DOCKET NO.: AREN-0315 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Dominic P. Behan et al.

Serial No.: **Group Art Unit:** unknown

Filing Date: January 23, 2002 **Examiner:** unknown

For: NON-ENDOGENEOUS, CONSTITUTIVELY ACTIVATED HUMAN SEROTONIN RECEPTORS AND SMALL MOLECULE MODULATORS THEREOF

Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Please make the following amendments to the above-identified application.

In the Sequence Listing:

Please delete the Sequence Listing on file and insert therefore pages 1-19 comprising the most recently filed Sequence Listing.

In the Specification:

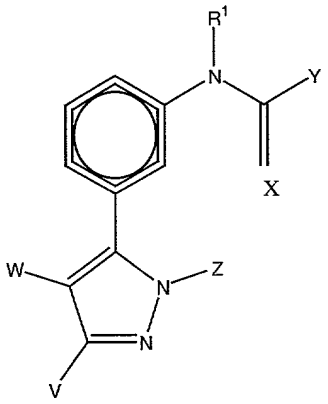
Please amend the paragraph on page 31, lines 2 to 7, to read as follows:

Based upon these results, structure activity analysis of the 103487 compound suggested that a series of derivatives of N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][{(4-trifluoromethoxy)phenyl}aminocarboxamide would exhibit similar 5-HT_{2A} activity and selectivity. A series of derivatives of N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][{(4-trifluoromethoxy)phenyl}aminocarboxamide were synthesized. These "directed" library

compounds (Tripos, Inc.) were then analyzed in accordance with the protocols of Examples 9c(1), 9c(2) and 9d.

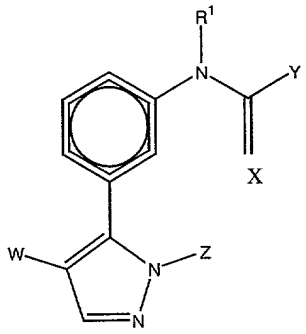
Please amend the paragraph on page 31, lines 8 to 12, to read as follows:

This series of compounds exhibits highly selective 5-HT2A activity. Accordingly, in the first aspect of the invention, a series of compounds exhibiting 5-HT_{2A} receptor activity that are useful as inverse agonists at such receptors is designated by the general formula (A):



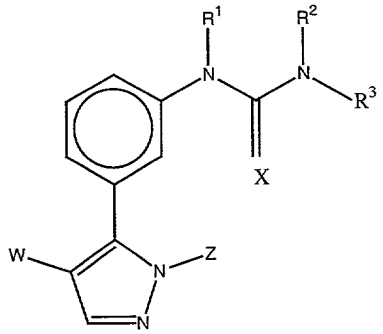
(A)

Please amend the paragraph on page 34, line 1, to read as follows:

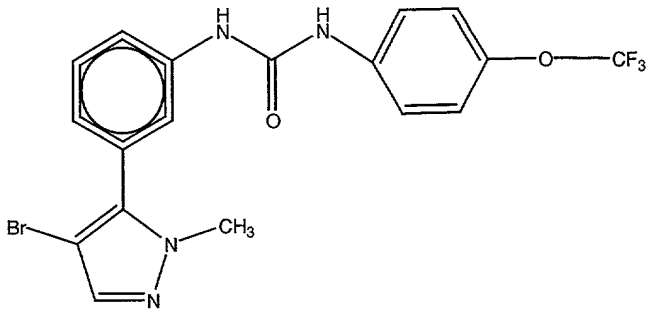


(B)

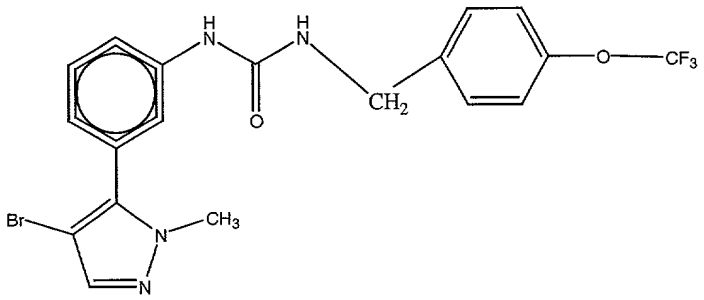
Please amend the paragraph on page 36, lines 9-10, to read as follows:



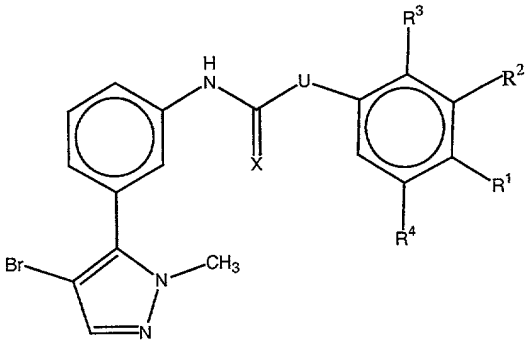
Please amend the paragraph on page 37, lines 3-4, to read as follows:



Please amend the paragraph on page 37, lines 8-9, to read as follows:



Please amend the paragraph on page 39, lines 1-2, to read as follows:



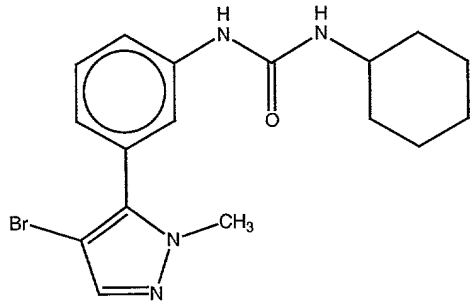
Please amend the paragraphs spanning pages 39 to page 41 to read as follows:

Compound No.	R^1	R^2	R^3	R^4	X	U	IP_3 % of Control	IP_3 AP-3 IC_{50} nM	WT $5HT_{2A}$ LSD IC_{50} nM
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][(4-methylthiophenyl)amino]carboxamide									
116079	SCH_3	H	H	H	O	NH	16	17	4
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][(4-chlorophenyl)amino]carboxamide									
116081	Cl	H	H	H	O	NH	10	3.2	11
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-(4-fluorophenyl)carboxamide									
116082	F	H	H	H	O	NH	11	-	7
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-[2-(trifluoromethoxy)phenyl]carboxamide									

116087	H	H	CF_3O	H	O	NH	11	-	200
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-(2-nitrophenyl)carboxamide									
116089	H	H	NO_2	H	O	NH	27	-	238
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-(4-methoxyphenyl)carboxamide									
116091	MeO	H	H	H	O	NH	12	-	19
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(2-methylphenyl)carboxamide									
116092	H	H	Me	H	O	NH	32	-	131
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-[4-(trifluoromethyl)phenyl] carboxamide									
116097	CF_3	H	H	H	O	NH	11	-	65
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-(3-chlorophenyl)carboxamide									
116105	H	Cl	H	H	O	NH	11	-	39
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-[2-chlorophenyl)carboxamide									
116108	H	H	Cl	H	O	NH	6	-	249
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-[4-(methylethyl)phenyl]carboxamide									
116110	isopropyl	H	H	H	O	NH	7	-	338
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-(3-methoxyphenyl)carboxamide									
116111	H	MeO	H	H	O	NH	7	-	106

[{3-(4-bromo-2-methylpyrazol-3-yl)phenyl}-amino]-N-(3-methylphenyl)carboxamide									
116112	H	Me	H	H	O	NH	14	-	57
[{3-(4-bromo-2-methylpyrazol-3-yl)phenyl}-amino]-N-methyl-N-[4-(trifluoromethoxy)phenyl]carboxamide									
116113	CF_3O	H	H	H	O	NCH_3	-	193	2
N-[4-(tert-butyl)phenyl]{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}carboxamide									
116119	t-butyl	H	H	H	O	NH	17	-	476
N-[4-(dimethylamino)phenyl]{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}carboxamide									
116122	NMe_2	H	H	H	O	NH	9	-	309
N-(3,5-dichloro-4-methylphenyl){[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}carboxamide									
116138	Me	Cl	H	Cl	O	NH	23	-	122
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-[4-(trifluoromethylthio)phenyl]carboxamide									
116139	CF_3S	H	H	H	O	NH	12	-	56
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-(2-fluorophenyl)carboxamide									
116144	H	H	F	H	O	NH	12	-	37

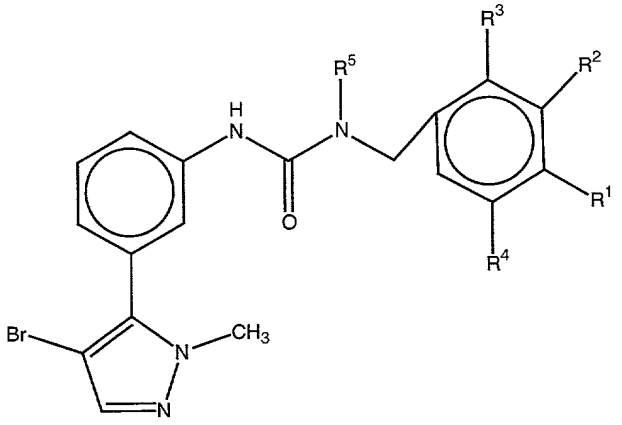
2-({[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}carbonylamino)benzamide									
116145	H	H	$CONH_2$	H	O	NH	31	-	7473
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-(4-cyanophenyl)carboxamide									
116147	CN	H	H	H	O	NH	12	-	2
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-(2-cyanophenyl)carboxamide									
116148	H	H	CN	H	O	NH	30	-	348



Please amend the table on page 42 to read as follows:

Compound No.		IP_3 AP-3 IC_{50} nM	WT $5HT_{2A}$ LSD IC_{50} nM
116141	N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-[cyclohexylamino]carboxamide	114	81

Please amend the paragraph on page 42, lines 3-4, to read as follows:

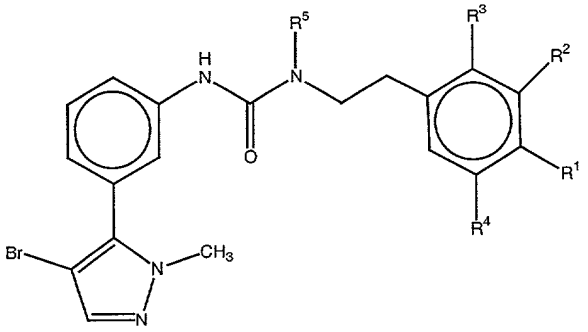


Please amend the table on page 42, lower, to 43, upper, to read as follows:

Compound No.	R^1	R^2	R^3	R^4	R^5	IP_3 AP-3	WT $5HT_{2A}$

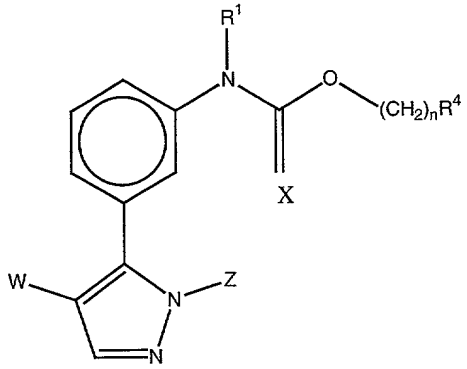
						IC_{50} nM	LSD IC_{50} nM
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-[phenylmethylamino]carboxamide							
116143	H	H	H	H	H	120	47
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-[{(4-fluorophenyl)methyl}amino]carboxamide							
116182	F	H	H	H	H	89	132
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]- [{(3,4-dimethoxyphenyl)methyl}amino]-carboxamide							
116183	OMe	OMe	H	H	H	-	1010
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-[{(3,4,5-trimethoxyphenyl)methyl}amino]-carboxamide							
116184	OMe	OMe	H	OMe	H	-	2960
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][{(2-methylphenyl)methyl}amino]carboxamide							
116185	H	H	Me	H	H	-	769
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][{(4-methoxyphenyl)methyl}amino]carboxamide							
116189	OMe	H	H	H	H	-	102

Please amend the paragraphs on pages 43-44, to read as follows:



Compound No.	R^1	R^2	R^3	R^4	R^5	IP_3 AP-3 IC_{50} nM	WT $5HT_{2A}$ LSD IC_{50} nM
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][{2-(4-methoxyphenyl)ethyl}amino]carboxamide							
116194	OMe	H	H	H	H	32	61

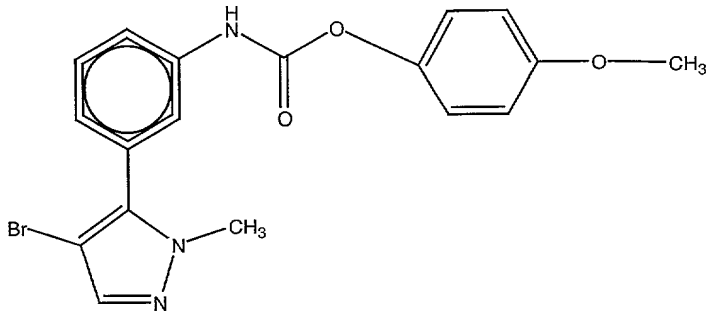
Please amend the paragraph on page 44, lines 7-8, to read as follows:



Please amend the paragraph on page 44, line 17, to page 45, line 2, to read as follows:

116100

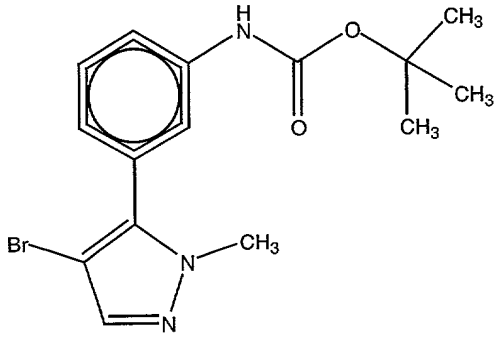
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][4-methoxyphenoxy]carboxamide



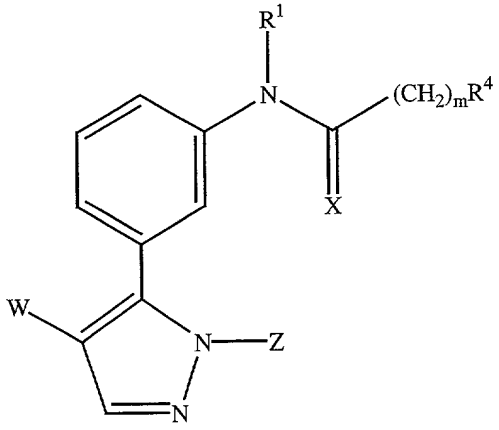
Please amend the paragraph on page 45, lines 6-7 to read as follows:

116192

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(1,1-dimethylethoxy)carboxamide



Please amend the paragraph on page 47, lines 3-4 to read as follows:

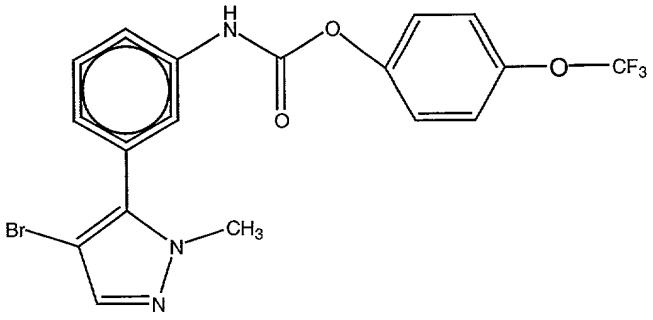


Please amend page 47, line 13, to page 49, line 1 to read as follows:

116101

m = 0, R^1 = H, R^4 = 4-trifluoromethoxyphenyl

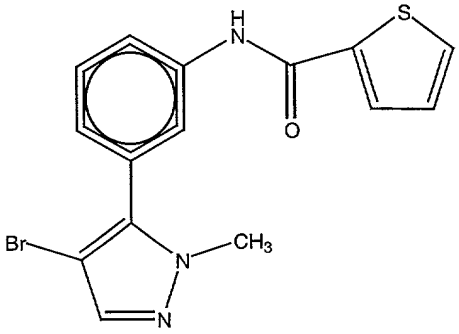
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][4-trifluoromethoxyphenyl]carboxamide



116102

m=0, R^1= H, R^4= thiophene

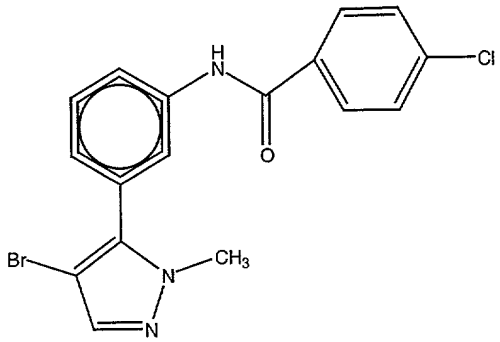
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][2-thienyl]carboxamide



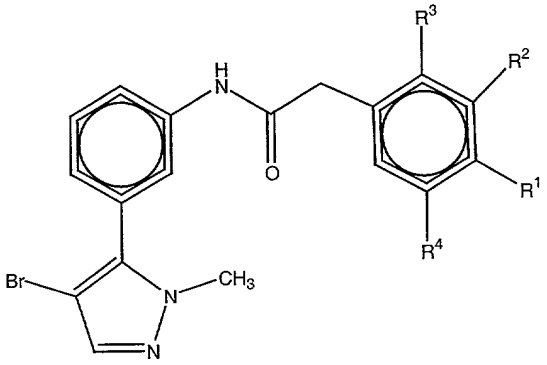
116120

m=0, R^1= H, R^4= chlorophenyl

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][4-chloro-phenyl]carboxamide



Please amend page 51, line 6, to page 52, line 1 to read as follows:

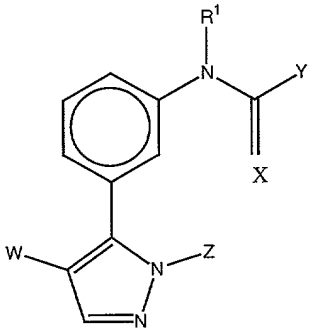


Name	Compound No.	R^1	R^2	R^3	R^4	IP_3 IC_{50} nM	LSD IC_{50} nM
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-[4-(trifluoromethoxy)-phenyl]acetamide	116137	OCF_3	H	H	H	-	106
N-[3-(4-bromo-2-methylpyrazol-3-	116174	H	F	H	H	153	318

yl)phenyl]-2-(3-fluorophenyl)acetamide							
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(3-methoxyphenyl)acetamide	116175	H	OMe	H	H	108	625
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(2-fluorophenyl)acetamide	116176	H	H	F	H	129	662
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(4-nitrophenyl)acetamide	116177	NO_2	H	H	H	61	108
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(2-methoxyphenyl)acetamide	116178	H	H	OMe	H	165	2300

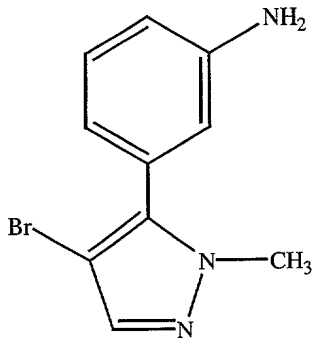
compound names not provided

Please amend the paragraph on page 52, line 7 to read as follows:



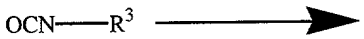
Please amend the paragraph on page 55, lines 5-13, to read as follows:

Compounds of general formula **(I)** can be obtained *via* a variety of synthetic routes all of which would be familiar to one skilled in the art. The reaction of isocyanates with amines is a commonly practiced method for the formation of ureas (see Org. Syn. Coll. Vol. V, (1973), 555). Amine (IV), 3-(4-bromo-2-methylpyrazole-3-yl)phenylamine, commercially available from Maybridge Chemical Company, Catalog No. KM01978, CAS No. 175201-77-1) reacts readily with isocyanates **(V)** in inert solvents such as halocarbons to yield the desired ureas of general formula **(I)** wherein $R^1 = R^2 = H$:

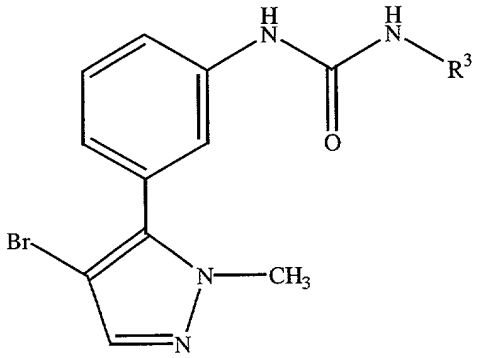


(IV)

+



(V)

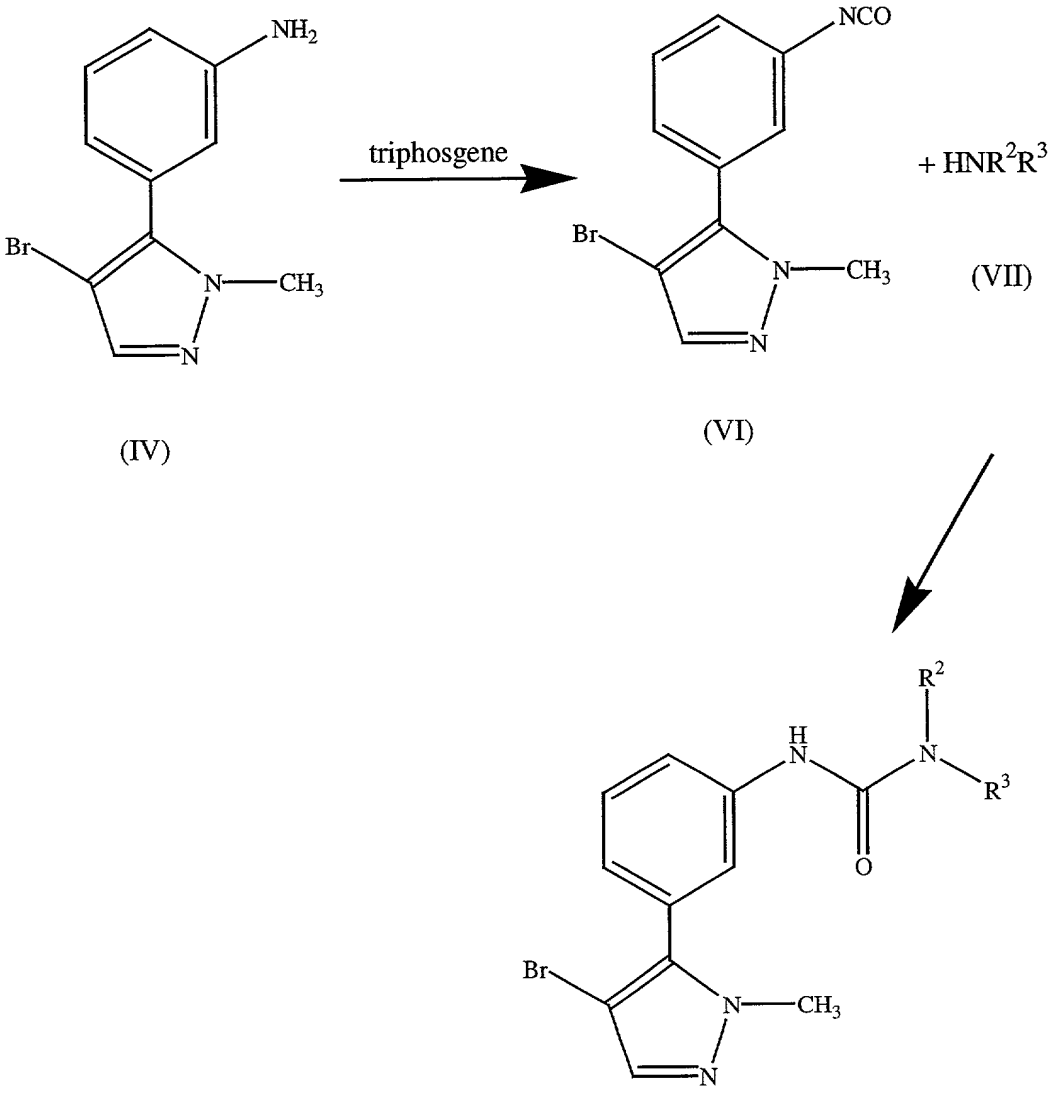


(I) $R^1 = R^2 = H$

Please amend the paragraph spanning page 55, line 14, to page 56, line 1, to read as follows:

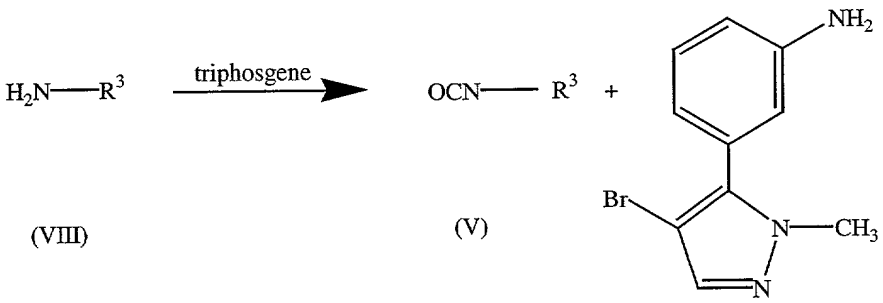
Alternatively the amine **(IV)** can be converted to the corresponding isocyanate

(VI) by the action of phosgene or a suitable phosgene equivalent, *e.g.* triphosgene, in an inert solvent such as a halocarbon in the presence of an organic base such as triethylamine or ethyldiisopropylamine. Isocyanate **(VI)** reacts with amines of general formula **(VII)**, in an analogous fashion to that described above for the reaction of **(IV)** with **(V)**, yielding the desired ureas of general formula **(I)** wherein R^1 = H:

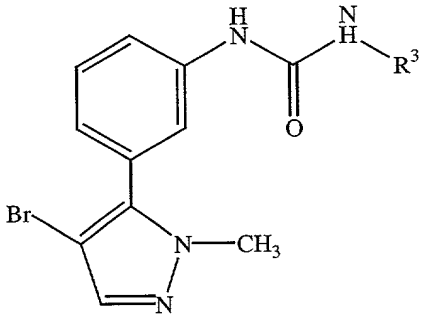


Please amend the paragraph spanning page 56, line 2, to page 57, line 1, to read as follows:

Alternatively wherein the isocyanate of general formula **(V)** is not commercially available it can be prepared from the corresponding amine of general formula **(VIII)** in an analogous procedure to that described above for the preparation of **(VI)**. Reaction of these isocyanates with **(IV)** would again yield the requisite ureas of general formula **(I)** wherein $R^1 = R^2 = H$:



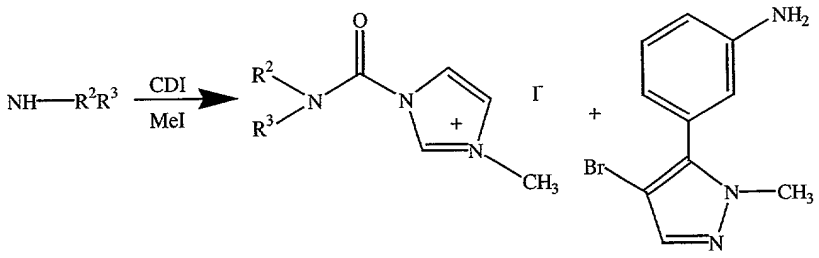
(VIII) (V) (VI)



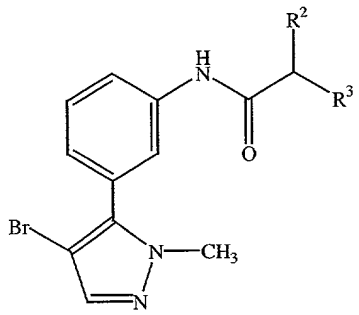
(I) $R^1 = R^2 = H$

Please amend the paragraph spanning page 57, line 2, to page 58, line 1, to read as follows:

Amines of general formula **(VII)** are also readily converted to activated isocyanate equivalents of general formula **(IX)** by the sequential action of carbonyldiimidazole and methyl iodide in tetrahydrofuran and acetonitrile respectively (R.A. Batey *et al*, *Tetrahedron Lett.*, (1998), 39, 6267-6270.) Reaction of **(IX)** with **(IV)** in an inert solvent such as a halocarbon would yield the requisite ureas of general formula **(I)** wherein R^1 = H:



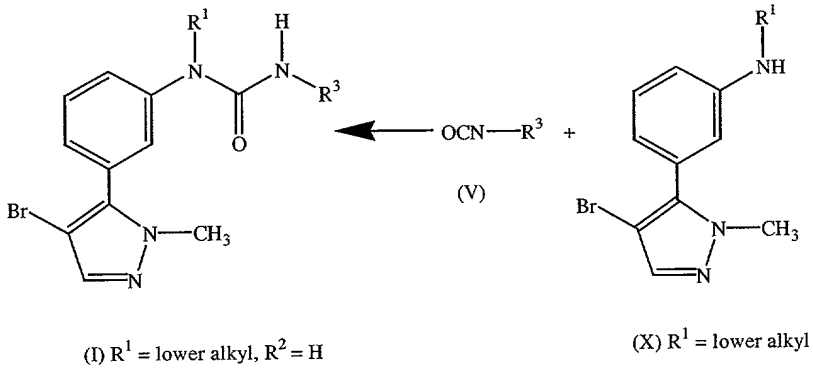
(VII) (IX) (IV)



(I) $R^1 = H$

Please amend the paragraph spanning page 58, line 2, to page 59, line 1, to read as follows:

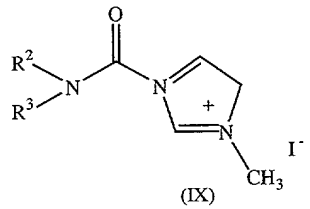
Amine **(IV)** may be monomethylated according to the procedure of J. Barluenga *et al*, *J. Chem. Soc., Chem. Commun.,* (1984), 20, 1334-1335, or alkylated according to the procedure of P. Marchini *et al*, *J. Org. Chem.,* (1975), 40(23), 3453-3456, to yield compounds of general formula **(X)** wherein R^1 = lower alkyl. These materials may be reacted as above with reagents of general formula **(V)** and **(IX)** as depicted below:



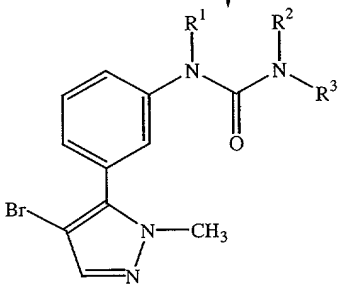
(I) R^1 = lower alkyl, R^2 = H

(X) R^1 = lower alkyl

+

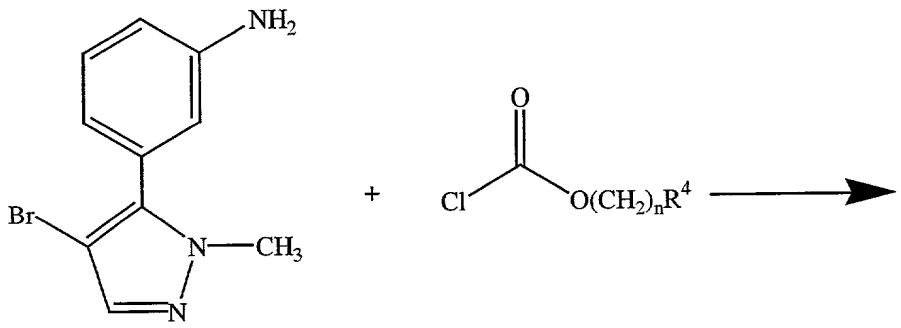


(IX)

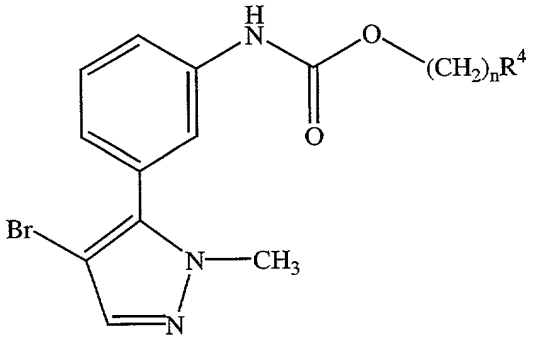


(I) R^1 = lower alkyl

Please amend the paragraph on page 60, line 3, to read as follows:

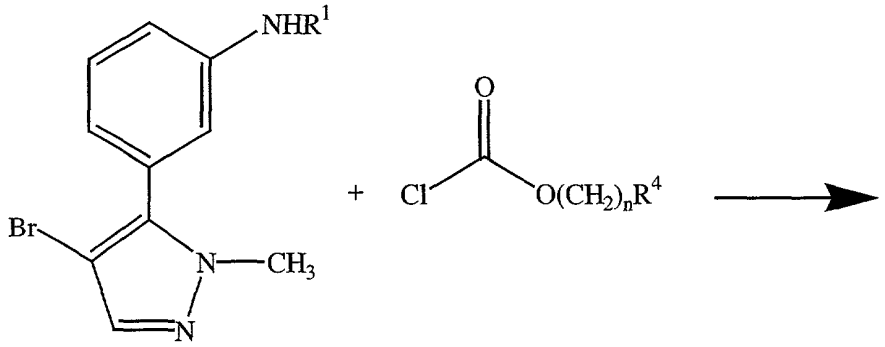


(IV)

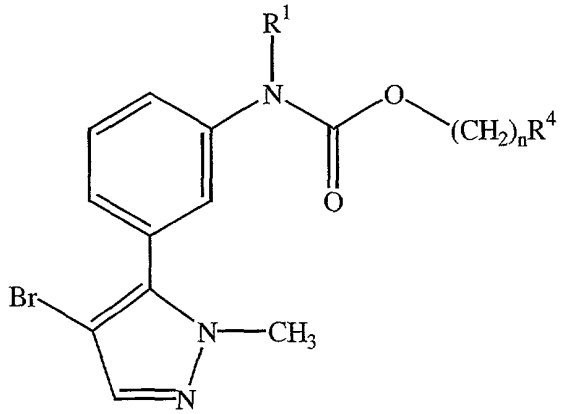


(II) $R^1 = H$

Please amend the paragraph on page 60, line 4, to read as follows:

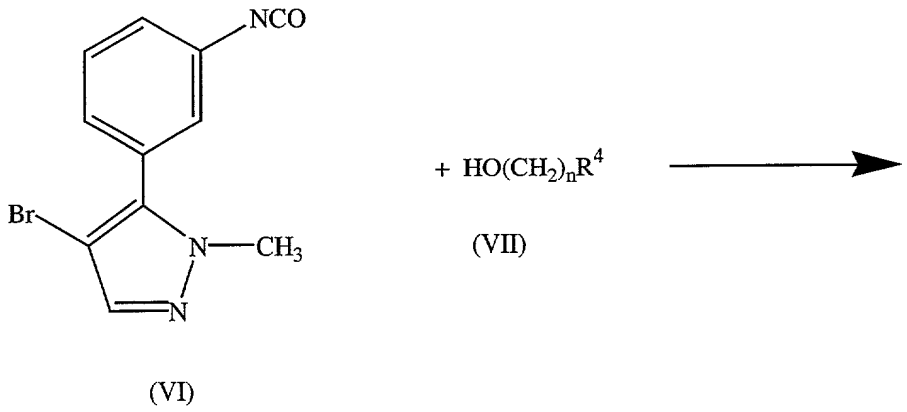


(X) R^1 = lower alkyl (XI)

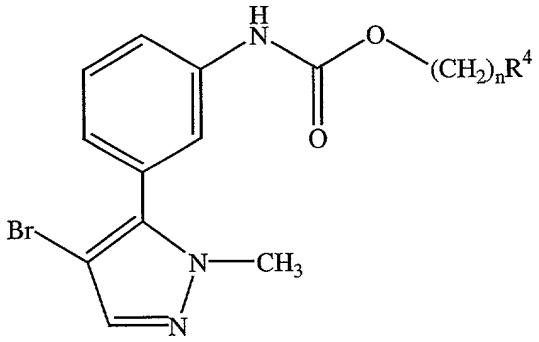


(II) R^1 = lower alkyl

Please amend the paragraph on page 61, line 1, to read as follows:

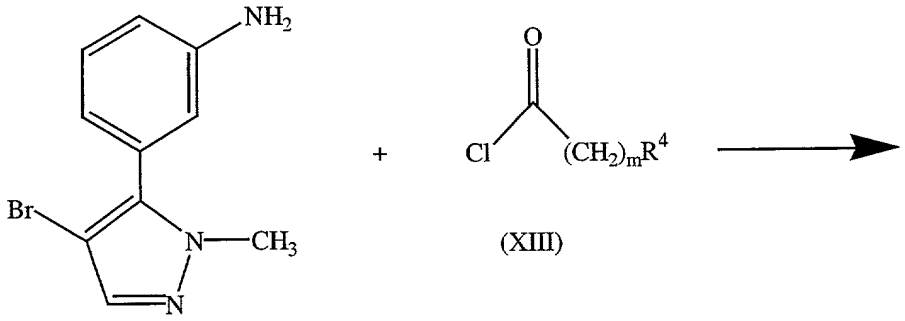


(VI)

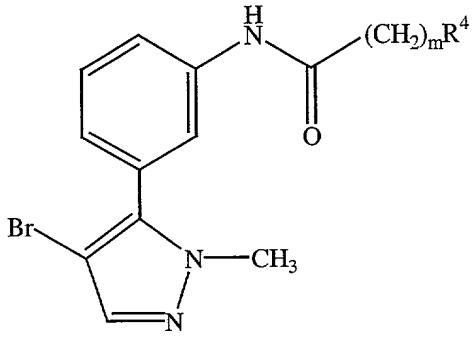


(II) $R^1 = H$

Please amend the paragraph on page 62, line 1, to read as follows:

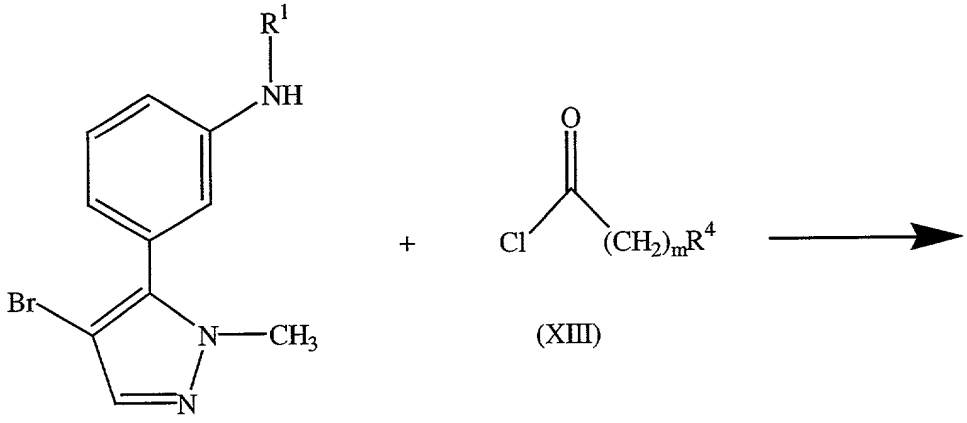


(IV) (XIII)



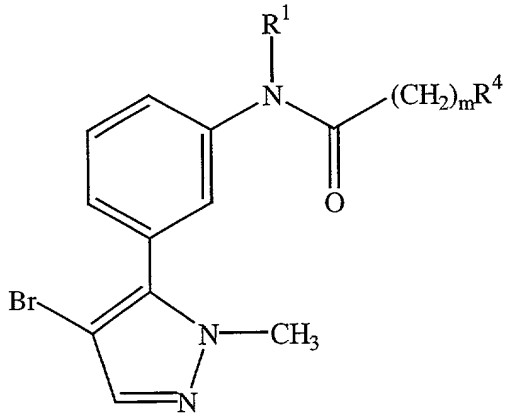
(III) $R^1 = H$

Please amend the paragraph on page 61, line 2, to read as follows:



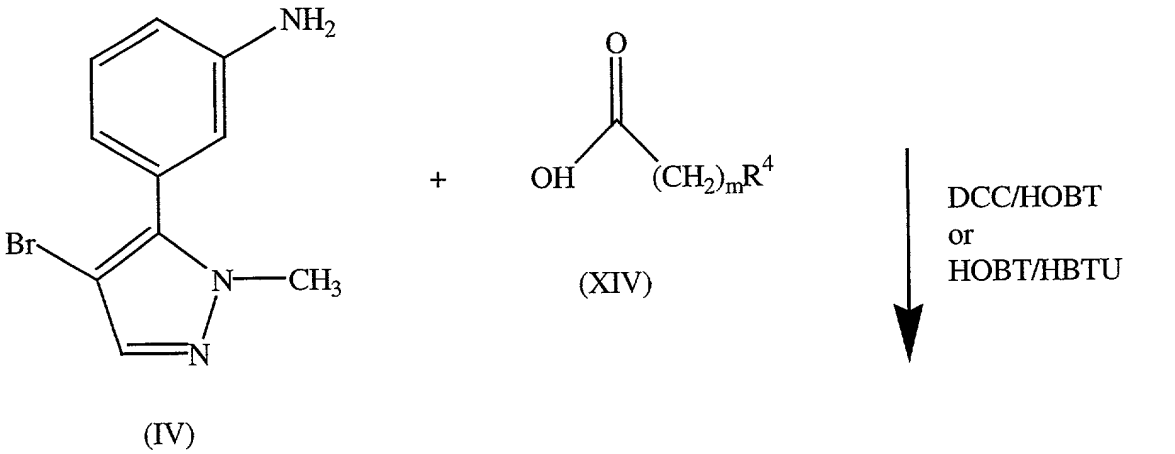
(X) R^1 = lower alkyl

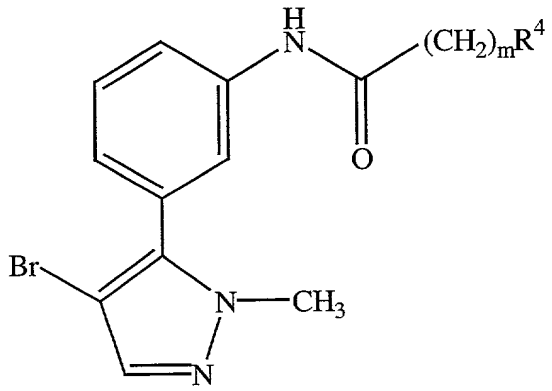
(XIII)



(III) R^1 = lower alkyl

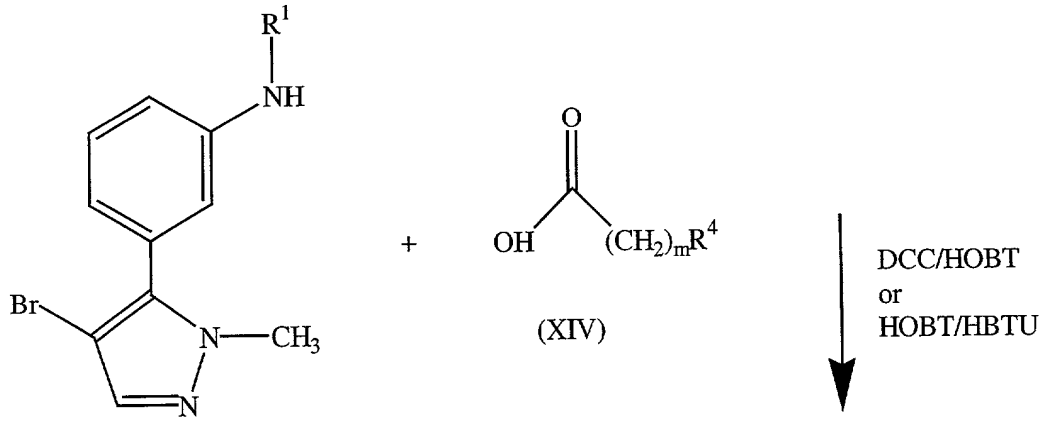
Please amend page 63, line 1 to read as follows:



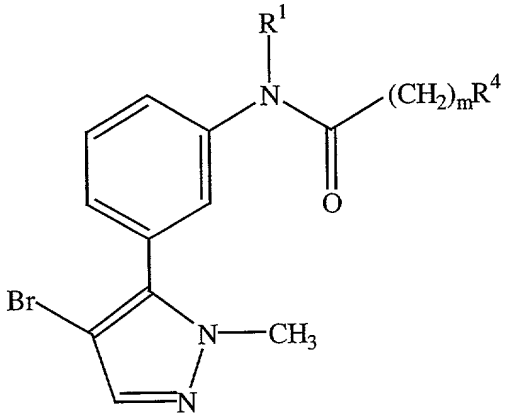


(III) $R^1 = H$

Please amend page 63, line 5, to read as follows:



(X) R^1 = lower alkyl



(III) R^1 = lower alkyl

Please amend the paragraph on page 66, line 28 to page 67, line 2, to read as follows:

Experiment 2

Preparation and Analysis of 116100

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][4-methoxyphenoxy]carboxamide

To 4-methoxyphenylchloroformate (19 mg, 0.10 mmol) in CH_2Cl_2 (0.5 mL) was added dropwise a solution 3-(3-aminophenyl)-4-bromo-2-methylpyrazole (25 mg, 0.10 mmol) and triethylamine (14 μL, 0.10 mmol) in CH_2Cl_2 (0.5 mL). The mixture was stirred for 16 h and concentrated. Chromatography on flash silica (40% EtOAc/hexane) gave the title compound as a colourless solid (21 mg, 52%), m.p. 140.3-141.8°C. (EtOAc/hexane).

Please amend the paragraph on page 67, lines 9-17, to read as follows:

Experiment 3

Preparation and Analysis of 116101

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][4-trifluoromethoxyphenyl]carboxamide

To 4-(trifluoromethoxy)benzoyl chloride (19 μL, 0.12 mmol) in CH_2Cl_2 (1 mL) was added dropwise a solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole (30 mg, 0.12 mmol) and triethylamine (17 μL, 0.12 mmol) in CH_2Cl_2 (0.5 mL). The reaction mixture was stirred for 16 h and concentrated. Chromatography on flash silica (50% EtOAc/hexane) gave the title compound as a colourless solid (40 mg, 76%), m.p. 138.6-139.6 °C (EtOAc/hexane).

Please amend the paragraph on page 67, lines 23-30, to read as follows:

Experiment 4

Preparation and Analysis of 116102

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][2-thienyl]carboxamide

To thiophene-2-carbonyl chloride (11 μL, 0.09 mmol) in CH_2Cl_2 (1 mL) was added dropwise a solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole (25 mg, 0.09 mmol) and triethylamine

(14 μL, 0.09 mmol) in CH_2Cl_2 (0.5 mL). The reaction mixture was stirred for 16 h and concentrated. Chromatography on flash silica (50% EtOAc/hexane) gave the title compound as a colourless solid (24 mg, 68%), m.p. 127.8-128.6 °C (EtOAc/hexane).

Please amend the paragraph on page 68, lines 5-14, to read as follows:

Experiment 5

Preparation and Analysis of 116115

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][{(4-trifluoromethoxy)phenyl)methyl}amino] carboxamide

To a stirred solution of triphosgene (12 mg, 0.04 mmol) in CH_2Cl_2 (0.5 mL) was added dropwise a solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole (30 mg, 0.12 mmol) and triethylamine (33 μL, 0.24 mmol) in CH_2Cl_2 (0.5 mL). After 1 h, 4-(trifluoromethoxy)benzylamine (23 mg, 0.12 mmol) was added. The reaction mixture was stirred for 16 h and concentrated. Chromatography on flash silica (75% EtOAc/hexane) gave the title compound as a colourless solid (38 mg, 68%), m.p. 144.6-145.8 °C (EtOAc/hexane).

Please amend the paragraph on page 68, lines 21-28, to read as follows:

Experiment 6

Preparation and Analysis of 116120

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][4-chlorophenyl]carboxamide

To 4-chlorobenzoyl chloride (15 mg, 0.08 mmol) in CH_2Cl_2 (1 mL) was added dropwise a solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole (21 mg, 0.08 mmol) and triethylamine (12 μL, 0.08 mmol) in CH_2Cl_2 (0.5 mL). The mixture was stirred for 16 h and concentrated. Chromatography on flash silica (50% EtOAc/hexane) gave the title compound as a colourless solid (23 mg, 72%), m.p. 184.4-184.8 °C (EtOAc/hexane).

Please amend the paragraph on page 69, lines 1-33, to read as follows:

Experiment 7

Preparation and Analysis of 116137

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-[4-(trifluoromethoxy)phenyl]acetamide

A solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole (35 mg, 0.14 mmol) and triethylamine (23 μL, 0.17 mmol) in DMF (0.5 mL) was added in one portion to a stirred solution of 4-trifluoromethoxyphenylacetic acid (31 mg, 0.14 mmol), HBTU (53 mg, 0.14 mmol) and HOBT (19 mg, 0.14 mmol) in DMF (1 mL). The mixture was heated at 70 °C for 24 h and then quenched with aqueous sodium bicarbonate solution. Ethyl acetate was added and the organic phase separated, washed with water (.times.3), brine, dried ($MgSO_4$) and evaporated. Chromatography on flash silica (50% EtOAc/hexane) gave the title compound as a colourless solid (43 mg, 68%). m.p. 141.2-142.5 °C (EtOAc/hexane).

Please amend the paragraph on page 69, lines 21-33, to read as follows:

Experiment 8

Preparation and Analysis of 116174

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(3-fluorophenyl)acetamide

A mixture of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole (30 mg, 0.12 mmol), 3-fluorophenylacetic acid (18 mg, 0.12 mmol), 1-hydroxybenzotriazole hydrate (16 mg, 0.12 mmol) and 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluoro-phosphate (46 mg, 0.12 mmol) were dissolved in chloroform (1.5 ml). N,N-Diisopropylethylamine (0.02 ml, 0.13 mmol) was added and the mixture stirred at room temperature for 16 h. The reaction mixture was then poured into brine and the organic layer washed with further brine, dried over magnesium sulphate and then concentrated in vacuo. The crude product was purified by column chromatography (ethyl acetate-toluene, 1:1), giving the title compound (12 mg, 26%). Rf 0.41 (ethyl acetate-toluene, 1:1).

Please amend the paragraph on page 70, lines 5-16, as follows:

Experiment 9

Preparation and Analysis of 116175

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(3-methoxyphenyl)acetamide

A solution of 3-methoxyphenylacetyl chloride (0.02 ml, 0.12 mmol) in dichloromethane (0.75 ml) was added dropwise at 0 °C to a solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole (30 mg, 0.12 mmol) and triethylamine (0.02 ml, 0.13 mmol) in dichloromethane (0.75 ml). The resulting mixture was stirred at room temperature for 16 h and then poured into brine. The organic layer was washed with more brine then dried over magnesium sulphate and concentrated in vacuo. The crude product was purified by column chromatography (ethyl acetate-toluene, 1:1), giving the title compound (9 mg, 19%). Rf 0.30 (ethyl acetate-toluene, 1:1).

Please amend the paragraph on page 71, lines 21-33, to read as follows:

Experiment 10

Preparation and Analysis of 116176

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(2-fluorophenyl)acetamide

A mixture of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole (30 mg, 0.12 mmol), 2-fluorophenylacetic acid (18 mg, 0.12 mmol), 1-hydroxybenzotriazole hydrate (16 mg, 0.12 mmol) and 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluoro-phosphate (46 mg, 0.12 mmol) were dissolved in chloroform (1.5 ml). N,N-Diisopropylethylamine (0.02 ml, 0.13 mmol) was added and the mixture stirred at room temperature for 16 h. The reaction mixture was then poured into brine and the organic layer washed with further brine, dried over magnesium sulphate and then concentrated in vacuo. The crude product was purified by column chromatography (ethyl acetate-toluene, 1:1), giving the title compound (15 mg, 32%). Rf 0.52 (ethyl acetate-toluene, 1:1).

Please amend the paragraph on page 71, lines 5-17, to read as follows:

Experiment 11

Preparation and Analysis of 116177

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(4-nitrophenyl)acetamide

A mixture of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole (30 mg, 0.12 mmol), 4-nitrophenylacetic acid (22 mg, 0.12 mmol), 1-hydroxybenzotriazole hydrate (16 mg, 0.12 mmol) and 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (46 mg, 0.12 mmol) were dissolved in chloroform (1.5 ml). N,N-Diisopropylethylamine (0.02 ml, 0.13 mmol) was added and the mixture stirred at room temperature for 16 h. The reaction mixture was then poured into brine and the organic layer washed with further brine, dried over magnesium sulphate and then concentrated in vacuo. The crude product was purified by column chromatography (ethyl acetate-toluene, 1:1), giving the title compound (9 mg, 18%). Rf 0.19 (ethyl acetate-toluene, 1:1).

Please amend the paragraph on page 71, line 22, to page 72, line 2, to read as follows:

Experiment 12

Preparation and Analysis of 116178

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(2-methoxyphenyl)acetamide

A mixture of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole (30 mg, 0.12 mmol), 2-methoxyphenylacetic acid (20 mg, 0.12 mmol), 1-hydroxybenzotriazole hydrate (16 mg, 0.12 mmol) and 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (46 mg, 0.12 mmol) were dissolved in chloroform (1.5 ml). N,N-Diisopropylethylamine (0.02 ml, 0.13 mmol) was added and the mixture stirred at room temperature for 16 h. The reaction mixture was then poured into brine and the organic layer washed with further brine, dried over magnesium sulphate and then concentrated in vacuo. The crude product was purified by column

chromatography (chloroform-methanol, 99:1), giving the title compound (18 mg, 38%) as a colourless solid. Rf 0.65 (chloroform-methanol, 98:2).

Please amend the paragraph on page 72, lines 8-15, to read as follows:

Experiment 13

Preparation and Analysis of 116192

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(1,1-dimethylethoxy)carboxamide

To di-tert-butyl dicarbonate (36 mg, 0.17 mmol) in methanol (1 mL) was added dropwise a solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole (42 mg, 0.17 mmol) in methanol (1 mL). The mixture was stirred for 16 h and concentrated. Chromatography on flash silica (40% EtOAc/hexane) gave the title compound as a colourless solid (29 mg, 49%) (EtOAc/hexane).

Please amend the paragraph on page 72, lines 22 to page 73, line 2, to read as follows:

One or the other (as indicated) of the two following synthetic protocols was used to generate each of the compounds below:

Protocol A:

To an isocyanate (1 mmol) in CH_2Cl_2 (4 mL) was added dropwise a solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole (1 mmol) in CH_2Cl_2 (4 mL). The mixture was stirred for 16 hours and concentrated. Chromatography on flash silica (20%-80% EtOAc/hexane) followed by recrystallisation gave the pure urea.

Protocol B:

To a stirred solution of triphosgene (0.33 mmol) in CH_2Cl_2 (4 mL) was added dropwise a solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole (1 mmol) and triethylamine (2 mmol) in CH_2Cl_2 (4 mL). After 1 hour, an aniline was added (1 mmol). The reaction mixture was stirred

for 16 hours and concentrated. Chromatography on flash silica (20%-80% EtOAc/hexane) followed by recrystallisation gave the pure urea.

Please amend the paragraph on page 73, lines 5-8, to read as follows:

Experiment 14

Preparation and Analysis of 116079

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][(4-methylthiophenyl)amino]carboxamide

Please amend the paragraph on page 73, lines 16-18, to read as follows:

Experiment 15

Preparation and Analysis of 116081

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][(4-chlorophenyl)amino]carboxamide

Please amend the paragraph on page 73, lines 29-31, to read as follows:

Experiment 16

Preparation and Analysis of 116082

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(4-fluorophenyl)carboxamide

Please amend the paragraph on page 74, lines 6-8, to read as follows:

Experiment 17

Preparation and Analysis of 116087

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-[2-(trifluoromethoxy)phenyl]carboxamide

Please amend the paragraph on page 74, lines 17-19, to read as follows:

Experiment 18

Preparation and Analysis of 116089

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(2-nitrophenyl)carboxamide

Please amend the paragraph on page 74, lines 29-31, to read as follows:

Experiment 19

Preparation and Analysis of 116091

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(4-methoxyphenyl)carboxamide

Please amend the paragraph on page 75, lines 7-9, to read as follows:

Experiment 20

Preparation and Analysis of 116092

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(2-methylphenyl)carboxamide

Please amend the paragraph on page 75, lines 18-20, to read as follows:

Experiment 21

Preparation and Analysis of 116097

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-[4-(trifluoromethyl)phenyl]carboxamide

Please amend the paragraph on page 75, lines 28-30, to read as follows:

Experiment 22

Preparation and Analysis of 116105

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(3-chlorophenyl)carboxamide

Please amend the paragraph on page 76, lines 8-10, to read as follows:

Experiment 23

Preparation and Analysis of 116108

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(2-chlorophenyl)carboxamide

Please amend the paragraph on page 76, lines 20-22, to read as follows:

Experiment 24

Preparation and Analysis of 116110

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-[4-(methylethyl)phenyl]carboxamide

Please amend the paragraph on page 76, lines 31-33, to read as follows:

Experiment 25

Preparation and Analysis of 116111

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(3-methoxyphenyl)carboxamide

Please amend the paragraph on page 77, lines 8-10, to read as follows:

Experiment 26

Preparation and Analysis of 116112

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(3-methylphenyl)carboxamide

Please amend the paragraph on page 77, lines 19-22, to read as follows:

Experiment 27

Preparation and Analysis of 116113

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-methyl-N-[4-(trifluoromethoxy)phenyl]-carboxamide

Please amend the paragraph on page 77, lines 30-32, to read as follows:

Experiment 28

Preparation and Analysis of 116119

N-[4-(tert-butyl)phenyl]{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}carboxamide

Please amend the paragraph on page 78, lines 8-10, to read as follows:

Experiment 29

Preparation and Analysis of 116122

N-[4-(dimethylamino)phenyl]{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}carboxamide

Please amend the paragraph on page 78, lines 19-21, to read as follows:

Experiment 30

Preparation and Analysis of 116138

N-(3,5-dichloro-4-methylphenyl){[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}carboxamide

Please amend the paragraph on page 78, lines 30-32, to read as follows:

Experiment 31

Preparation and Analysis of 116139

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-[4-(trifluoromethylthio)phenyl]carboxamide

Please amend the paragraph on page 79, lines 8-10, to read as follows:

Experiment 32

Preparation and Analysis of 116141

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(cyclohexyl)carboxamide

Please amend the paragraph on page 79, lines 21-23, to read as follows:

Experiment 33

Preparation and Analysis of 116143

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(phenylmethyl)carboxamide

Please amend the paragraph on page 80, lines 1-3, to read as follows:

Experiment 34

Preparation and Analysis of 116144

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(2-fluorophenyl)carboxamide

Please amend the paragraph on page 80, lines 11-13, to read as follows:

Experiment 35

Preparation and Analysis of 116145

2-({[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}carbonylamino)benzamide

Please amend the paragraph on page 80, lines 21-23, to read as follows:

Experiment 36

Preparation and Analysis of 116147

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(4-cyanophenyl)carboxamide

Please amend the paragraph on page 80, lines 31-33, to read as follows:

Experiment 37

Preparation and Analysis of 116148

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(2-cyanophenyl)carboxamide

Please amend the paragraph on page 81, lines 9-11, to read as follows:

Experiment 38

Preparation and Analysis of 116182

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(4-fluorophenylmethyl)carboxamide

Please amend the paragraph on page 81, lines 21-23, to read as follows:

Experiment 39

Preparation and Analysis of 116183

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(3,4-dimethoxyphenylmethyl)carboxamide

Please amend the paragraph on page 82, lines 1-3, to read as follows:

Experiment 40

Preparation and Analysis of 116184

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(3,4,5-trimethoxyphenylmethyl)carboxamide

Please amend the paragraph on page 82, lines 13-15, to read as follows:

Experiment 41

Preparation and Analysis of 116185

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-[{(2-methylphenyl)methyl}amino]carboxamide

Please amend the paragraph on page 826, lines 25-27, to read as follows:

Experiment 42

Preparation and Analysis of 116189

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(4-methoxyphenylmethyl)carboxamide

Please amend the paragraph on page 83, lines 6-8, to read as follows:

Experiment 43

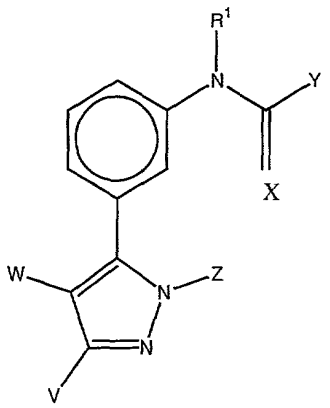
Preparation and Analysis of 116194

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-[2-(4-methoxy)phenylethyl]carboxamide

In the Claims:

Please delete claim 1. Please add new claims 14-26.

14. **(New)** A method for modulating by inverse agonism the activity of a human $5HT_{2A}$ serotonin receptor by contacting the receptor with a compound of formula:



Wherein:

W is lower alkyl (C_{1-6}), or halogen;

V is lower alkyl (C_{1-6}), or halogen;

X is either Oxygen or Sulfur;

Y is NR^2R^3, or $(CH_2)_mR^4$, or $O(CH_2)_nR^4$;

Z is lower alkyl (C_{1-6});

m=0-4

n=0-4

R^1 is H or lower alkyl(C_{1-4});

R^2 is H or lower alkyl(C_{1-4});

R^3 and R^4 are independently a C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, OCF_3, SMe, $COOR^7$, $SO_2NR^5R^6$, SO_3R^7, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, and aryloxy wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, or aryloxy groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, SO_3R^7, $SO_2NR^5R^6$, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl;

R^5 and R^6 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH_2 aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^7R^8$, NR^7R^8, $NHCOCH_3$, OCF_3, SMe, $COOR^9$, SO_3R^7, $SO_2NR^7R^8$, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, or aryl groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^8R^9$, N R^8R^9, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl,

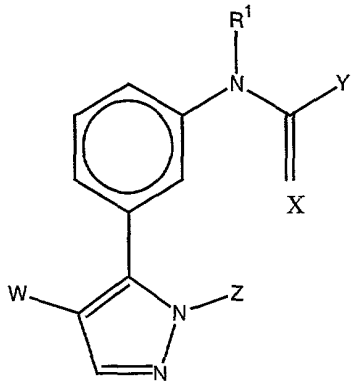
or R^5 and R^6 may form part of a 5, 6 or 7 membered cyclic structure which may be either saturated or unsaturated and that may contain up to four heteroatoms selected from O, N or S and said cyclic structure may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, Me, NO_2, OH, OMe, OEt, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, $HCOCH_3$, COEt, COMe, or halogen;

R^7 may be independently selected from H or C_{1-6} alkyl;

R^8 and R^9 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH_2 aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from halogen, CF_3, OCF_3, OEt, CCl_3, Me, NO_2, OH, OMe, SMe, COMe, CN , $COOR^7$, SO_3R^7, COEt, $NHCOCH_3$, or aryl;

an aryl moiety can be a 5 or 6 membered aromatic hetero-cyclic ring (containing up to 4 hetero atoms independently selected from N, O, or S) or a 6 membered aromatic non-heterocyclic ring or a polycycle.

15. **(New)** A method for modulating by inverse agonism the activity of a human $5HT_{2A}$ serotonin receptor by contacting the receptor with a compound of formula:



(B)

Wherein:

W is Me, or Et, or halogen;

X is either Oxygen or Sulfur;

Y is NR^2R^3, or $(CH_2)_mR^4$, or $O(CH_2)_nR^4$;

Z is lower alkyl (C_{1-6});

m=0-4

n=0-4

R^1 is H or lower alkyl (C_{1-4});

R^2 is H or lower alkyl(C_{1-4});

R^3 and R^4 are independently a C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, OCF_3, SMe, $COOR^7$, $SO_2NR^5R^6$, SO_3R^7, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, and aryloxy wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, or aryloxy groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, SO_3R^7, $SO_2NR^5R^6$, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl;

R^5 and R^6 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH, aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^7R^8$, NR^7R^8, $NHCOCH_3$, OCF_3, SMe, $COOR^9$, SO_3R^7, $SO_2NR^7R^8$, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, or aryl groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3 CCl_3, NO_2, OH, $CONR^8R^9$, NR^8R^9, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl,

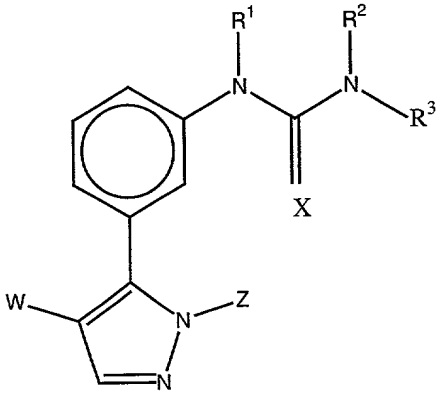
or R^5 and R^6 may form part of a 5, 6 or 7 membered cyclic structure which may be either saturated or unsaturated and that may contain up to four heteroatoms selected from 0, N or S and said cyclic structure may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, Me, NO_2, OH, OMe, OEt, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, $NHCOCH_3$, COEt, COMe, or halogen;

R^7 may be independently selected from H or C_{1-6} alkyl;

R^8 and R^9 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH_2aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from halogen, CF_3, OCF_3, OEt, CCl_3, Me, NO_2, OH, OMe, SMe, COMe, CN , $COOR^7$, SO_3R^7, COEt, $NHCOCH_3$, or aryl;

an aryl moiety can be a 5 or 6 membered aromatic hetero-cyclic ring (containing up to 4 hetero atoms independently selected from N, O, or S) or a 6 membered aromatic non-heterocyclic ring or a polycycle.

16. **(New)** A method for modulating by inverse agonism the activity of a human $5HT_{2A}$ serotonin receptor by contacting the receptor with a compound of formula:



(I)

Wherein:

R1 and R2 are H;

W is Br;

X is O;

Z is Me;

R^3 is C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, OCF_3, SMe, $COOR^7$, $SO_2NR^5R^6$, SO_3R^7, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, and aryloxy wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, or aryloxy groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, SO_3R^7, $SO_2NR^5R^6$, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl; R^5 and R^6 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH, aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^7R^8$, NR^7R^8, $NHCOCH_3$, OCF_3, SMe, $COOR^9$, SO_3R^7, $SO_2NR^7R^8$, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, or aryl groups may be further optionally substituted by up to four substituents in any position

independently selected from CF_3 CCl_3, NO_2, OH, $CONR^8R^9$, NR^8R^9, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl,

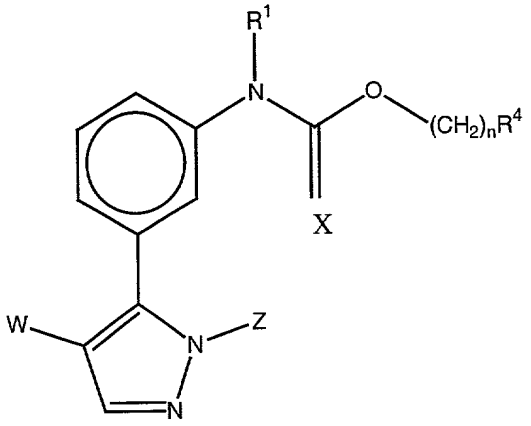
or R^5 and R^6 may form part of a 5, 6 or 7 membered cyclic structure which may be either saturated or unsaturated and that may contain up to four heteroatoms selected from 0, N or S and said cyclic structure may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, Me, NO_2, OH, OMe, OEt, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, $NHCOCH_3$, COEt, COMe, or halogen;

R^7 may be independently selected from H or C_{1-6} alkyl;

R^8 and R^9 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH_2aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from halogen, CF_3, OCF_3, OEt, CCl_3, Me, NO_2, OH, OMe, SMe, COMe, CN , $COOR^7$, SO_3R^7, COEt, $NHCOCH_3$, or aryl;

an aryl moiety can be a 5 or 6 membered aromatic hetero-cyclic ring (containing up to 4 hetero atoms independently selected from N, O, or S) or a 6 membered aromatic non-heterocyclic ring or a polycycle.

17. **(New)** A method for modulating by inverse agonism the activity of a human $5HT_{2A}$ serotonin receptor by contacting the receptor with a compound of formula:



(II)

Wherein:

W is Br;

X is O;

Z is Me;

R1 is H

M= 0 – 4;

R^4 is C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, OCF_3, SMe, $COOR^7$, $SO_2NR^5R^6$, SO_3R^7, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, and aryloxy wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, or aryloxy groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, SO_3R^7, $SO_2NR^5R^6$, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl;

R^5 and R^6 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH, aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^7R^8$, NR^7R^8, $NHCOCH_3$, OCF_3, SMe, $COOR^9$, SO_3R^7, $SO_2NR^7R^8$, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens,

C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, or aryl groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3 CCl_3, NO_2, OH, $CONR^8R^9$, NR^8R^9, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl,

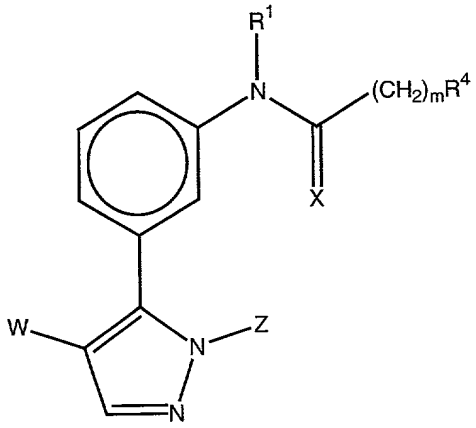
or R^5 and R^6 may form part of a 5, 6 or 7 membered cyclic structure which may be either saturated or unsaturated and that may contain up to four heteroatoms selected from 0, N or S and said cyclic structure may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, Me, NO_2, OH, OMe, OEt, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, $NHCOCH_3$, COEt, COMe, or halogen;

R^7 may be independently selected from H or C_{1-6} alkyl;

R^8 and R^9 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH_2aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from halogen, CF_3, OCF_3, OEt, CCl_3, Me, NO_2, OH, OMe, SMe, COMe, CN , $COOR^7$, SO_3R^7, COEt, $NHCOCH_3$, or aryl;

an aryl moiety can be a 5 or 6 membered aromatic hetero-cyclic ring (containing up to 4 hetero atoms independently selected from N, O, or S) or a 6 membered aromatic non-heterocyclic ring or a polycycle.

18. **(New)** A method for modulating by inverse agonism the activity of a human $5HT_{2A}$ serotonin receptor by contacting the receptor with a compound of formula:



wherein:

W is Br;

X is O;

Z is Me;

R1 is H;

m= 0-4;

R^4 is C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, OCF_3, SMe, $COOR^7$, $SO_2NR^5R^6$, SO_3R^7, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, and aryloxy wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, or aryloxy groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, SO_3R^7, $SO_2NR^5R^6$, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl;

R^5 and R^6 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH, aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^7R^8$, NR^7R^8, $NHCOCH_3$, OCF_3, SMe, $COOR^9$, SO_3R^7, $SO_2NR^7R^8$, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, or

aryl groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3 CCl_3, NO_2, OH, $CONR^8R^9$, NR^8R^9, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl,

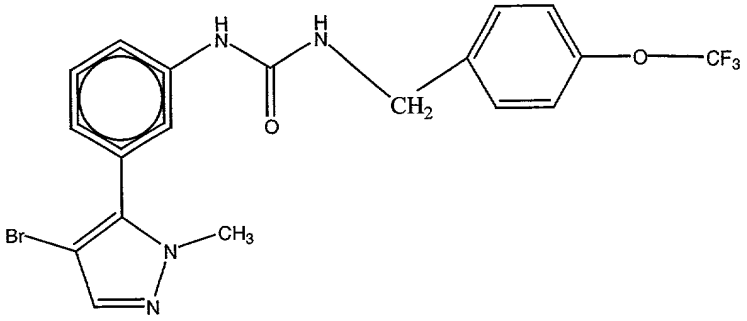
or R^5 and R^6 may form part of a 5, 6 or 7 membered cyclic structure which may be either saturated or unsaturated and that may contain up to four heteroatoms selected from 0, N or S and said cyclic structure may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, Me, NO_2, OH, OMe, OEt, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, $NHCOCH_3$, COEt, COMe, or halogen;

R^7 may be independently selected from H or C_{1-6} alkyl;

R^8 and R^9 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH_2aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from halogen, CF_3, OCF_3, OEt, CCl_3, Me, NO_2, OH, OMe, SMe, COMe, CN , $COOR^7$, SO_3R^7, COEt, $NHCOCH_3$, or aryl;

an aryl moiety can be a 5 or 6 membered aromatic hetero-cyclic ring (containing up to 4 hetero atoms independently selected from N, O, or S) or a 6 membered aromatic non-heterocyclic ring or a polycycle.

19. **(New)** The method of any one of claims 14-18 wherein the compound is selected from the group consisting of:



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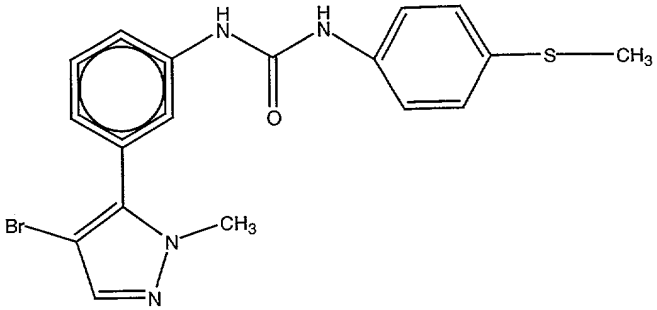

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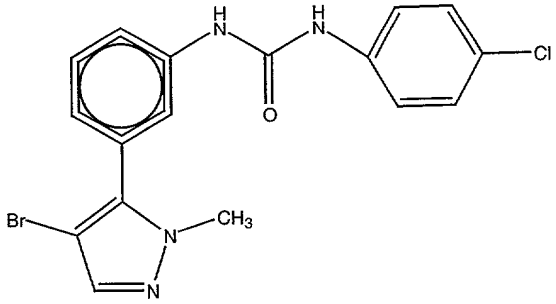

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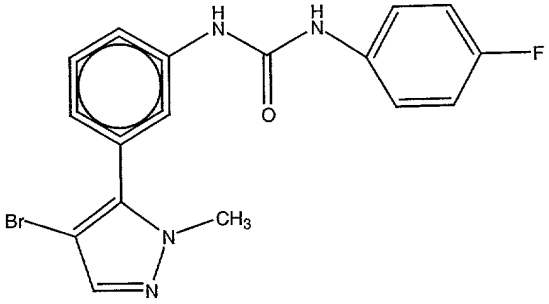

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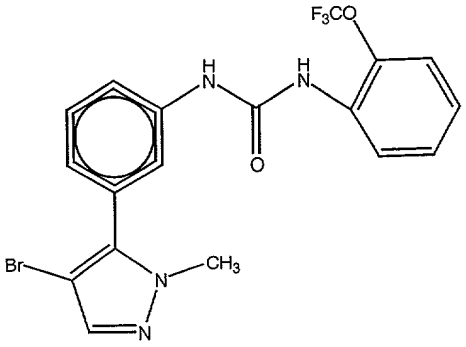
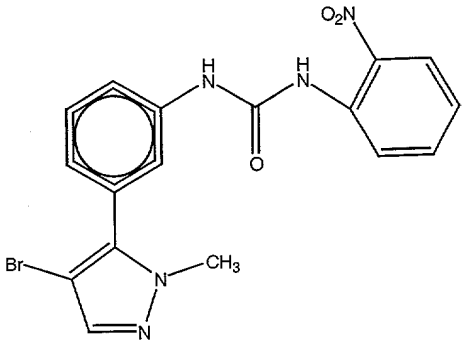

F3CO
H
N
H
N
O
Br
N
CH3
N

,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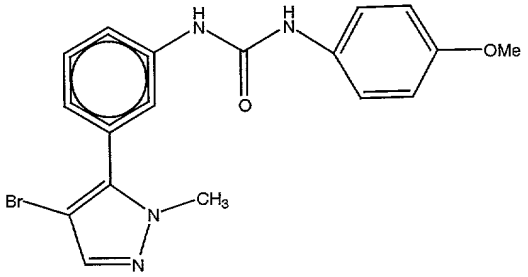
H
N
H
N
O
Br
N
CH3
N

,


H
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OMe
O
Br
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CH3
N

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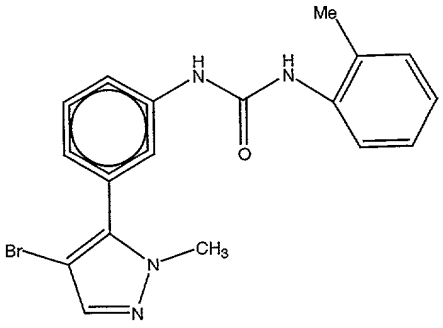
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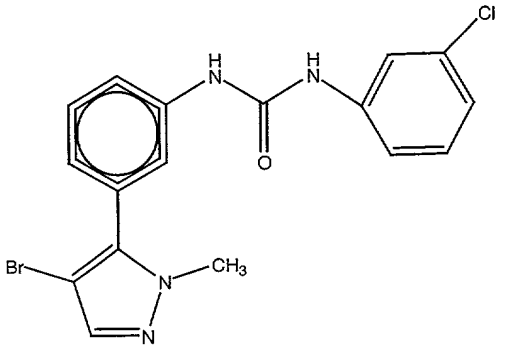
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Br
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CH3
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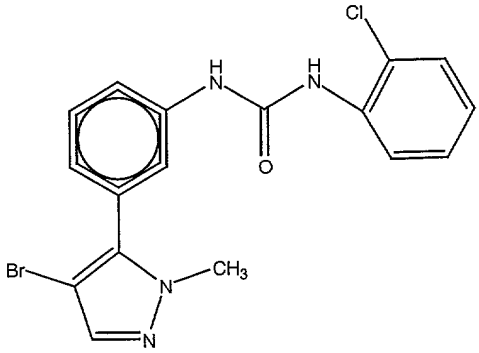
Cl
H
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H
N
O
Br
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CH3
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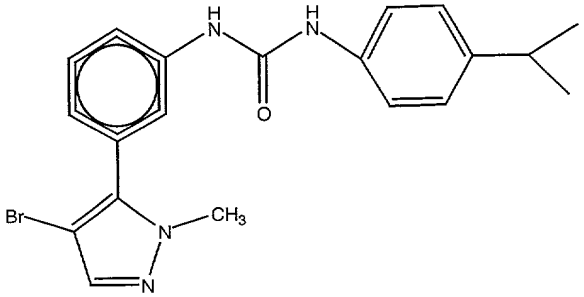
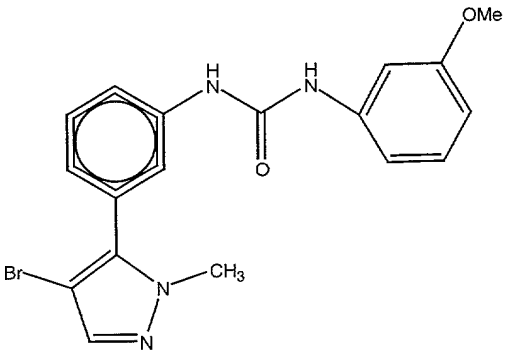

H
N
H
N
O
Br
N
CH3
N

,


OMe
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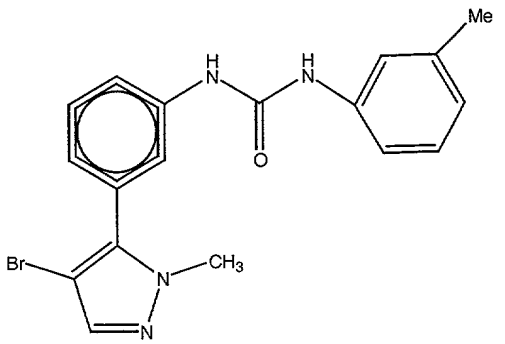
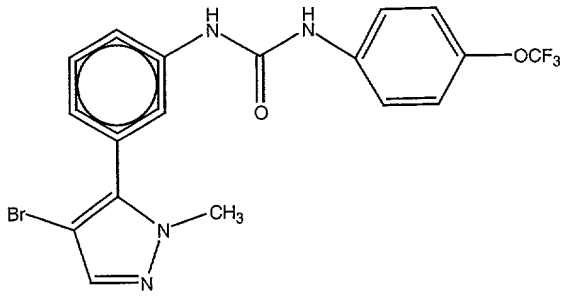
N
H
N
O
Br
N
CH3
N

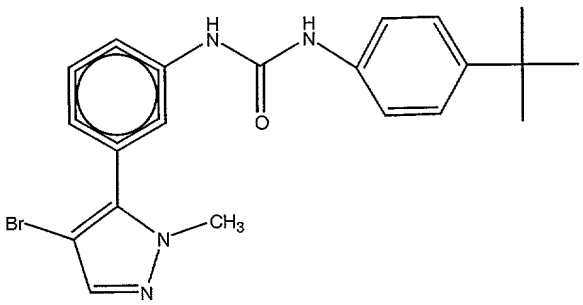
,


Me
H
N
H
N
O
Br
N
CH3
N

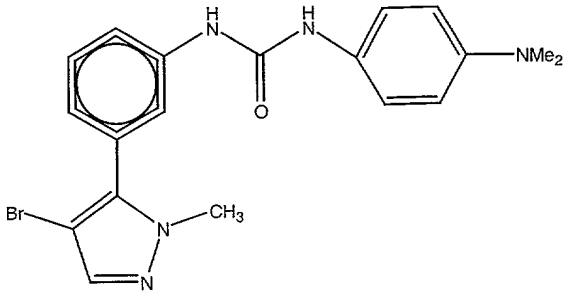
,


H
N
H
N
OCF3
O
Br
N
CH3
N

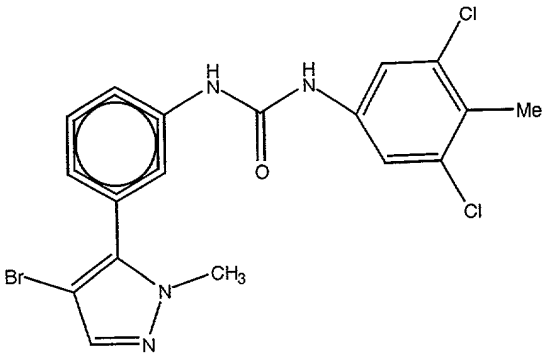
,


H
N
H
N
O
Br
N
CH3
N

,


H
N
H
N
NMe2
O
Br
N
CH3
N

,



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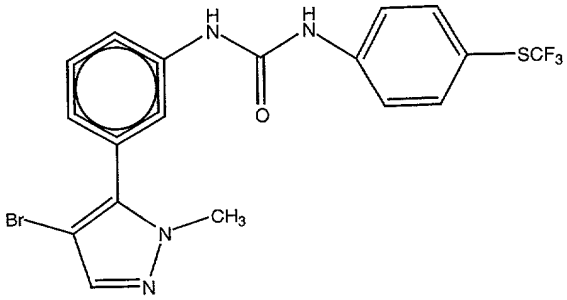

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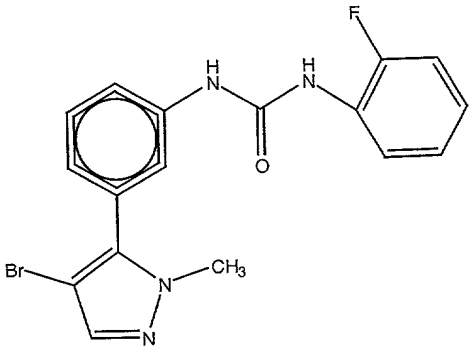

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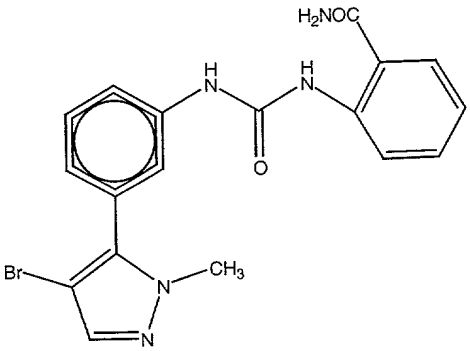

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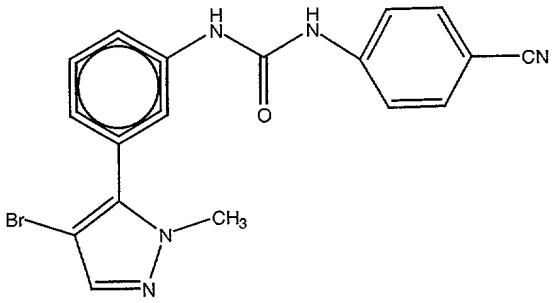

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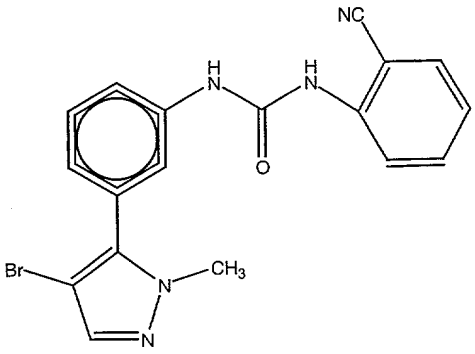

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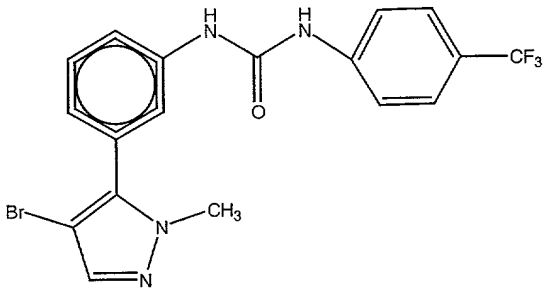

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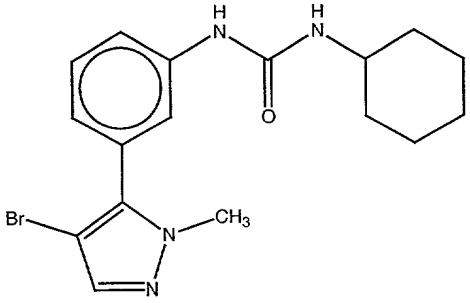

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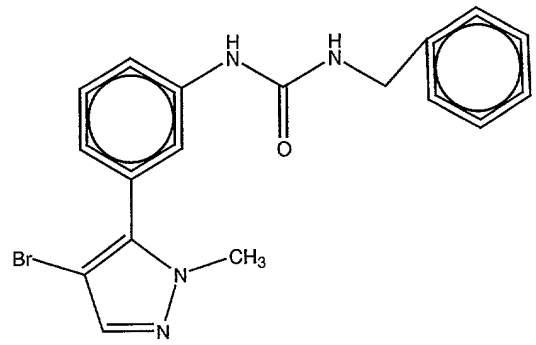
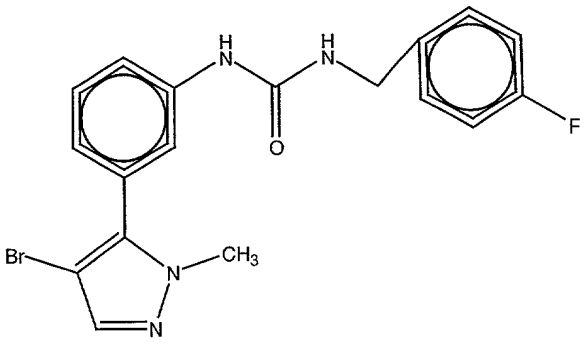

H
N
H
N
O
Br
N
CH3
N

,


H
N
H
N
O
F
Br
N
CH3
N

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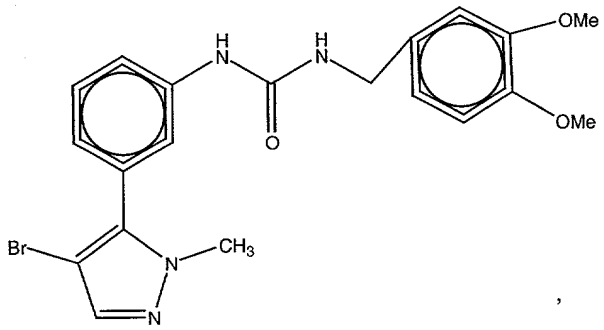
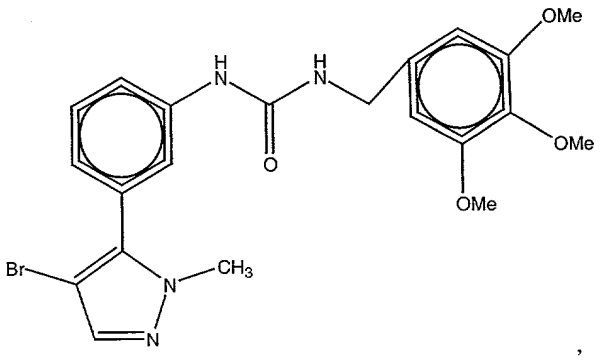
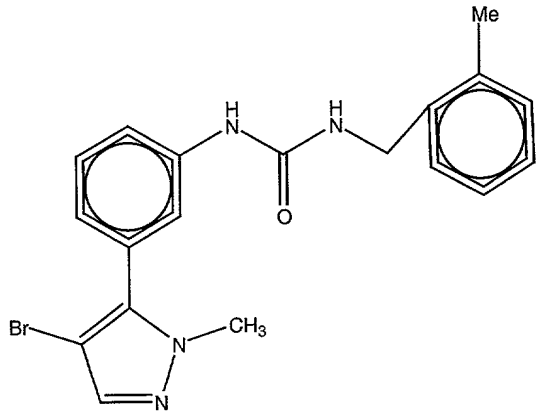

H
N
H
N
O
OMe
OMe
Br
N
CH3
N

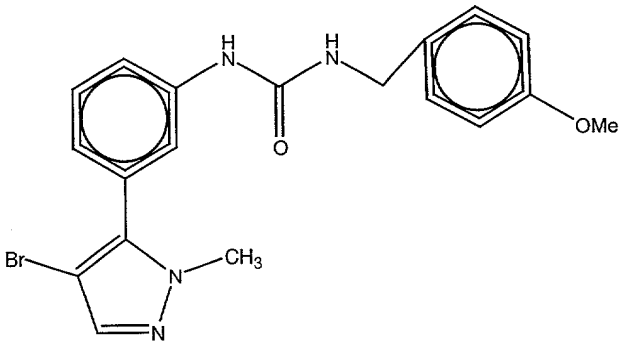
,


H
N
H
N
O
OMe
OMe
OMe
Br
N
CH3
N

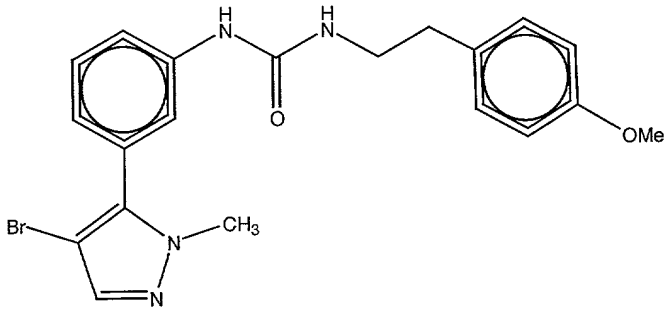
,


Me
H
N
H
N
O
Br
N
CH3
N

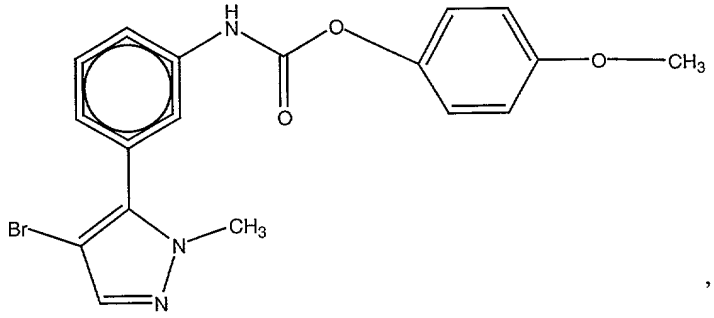
,


H
N
H
N
O
OMe
Br
N
CH3
N

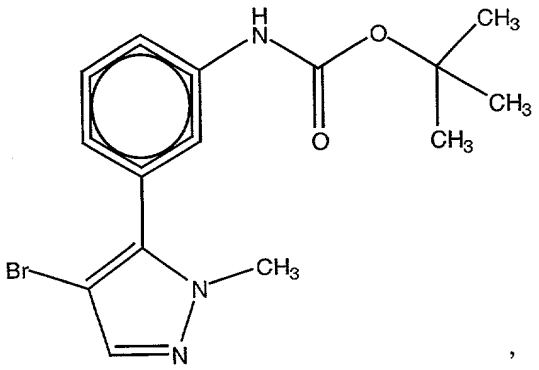
,


H
N
H
N
O
OMe
Br
N
CH3
N

,


H
N
O
O
O
CH3
Br
N
CH3
N

,



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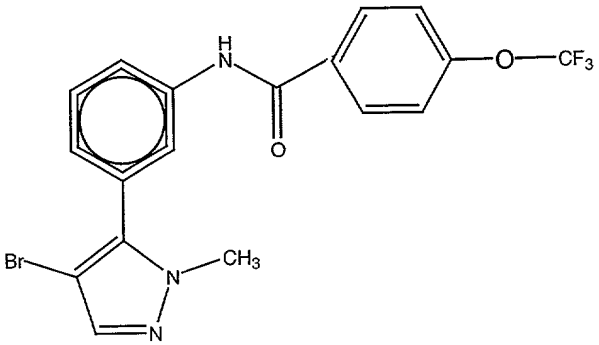

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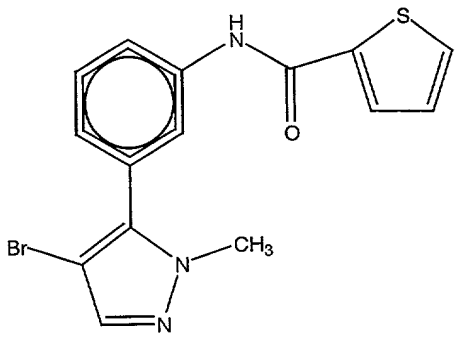

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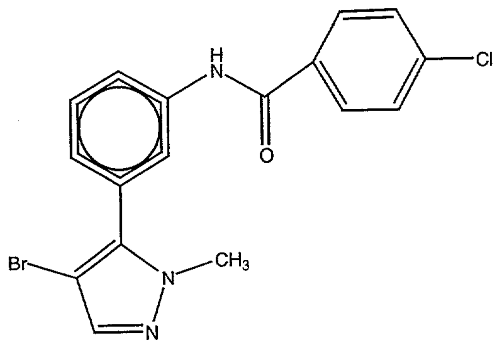
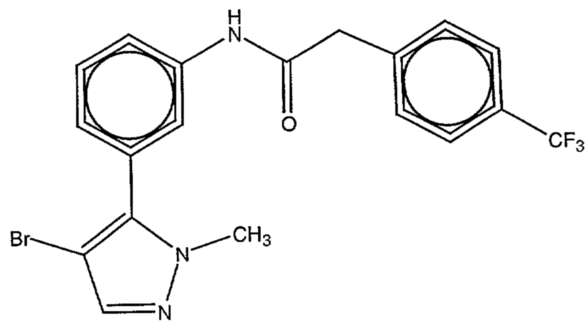
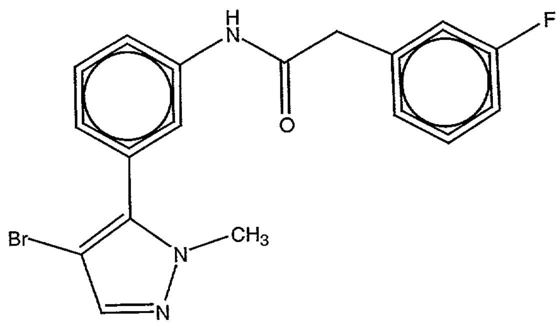

H
N
Cl
O
Br
N
CH3
N

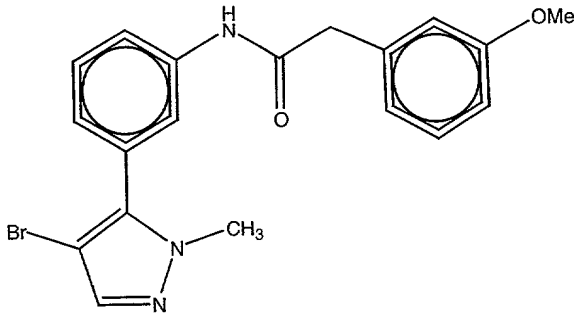
,


H
N
O
CF3
Br
N
CH3
N

,


H
N
F
O
Br
N
CH3
N

,


H
N
OMe
O
Br
CH3
N
N

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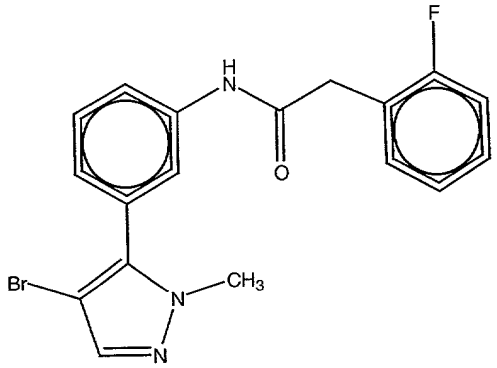
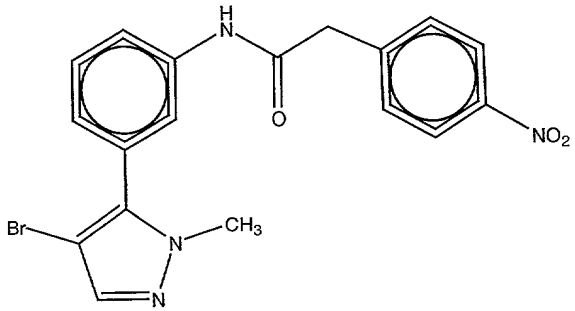
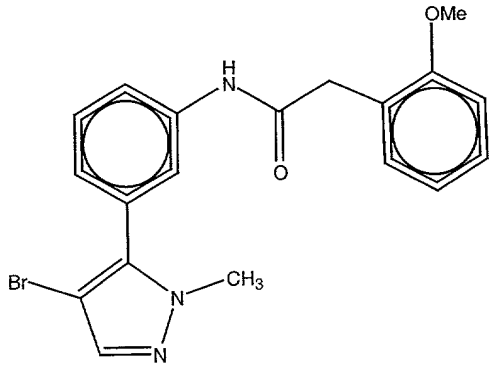

F
H
N
O
Br
CH3
N
N

,


H
N
O
NO2
Br
CH3
N
N

, or


OMe
H
N
O
Br
CH3
N
N

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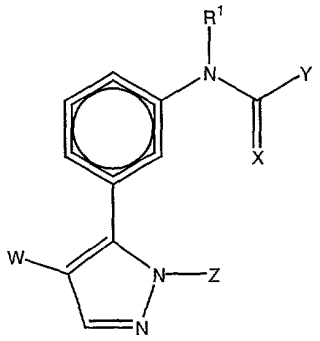
20. **(New)** A compound of formula (C):



(C)

Wherein:

W is Me, or Et, or halogen;

X is either Oxygen or Sulfur;

Y is NR^2R^3, or $(CH2)_m R^4$, or $O(CH_2)_n R^4$;

Z is lower alkyl (C_{1-6});

m=0-4;

n=0-4;

R^1 is H or lower alkyl (C_{1-4});

R^2 is H or lower alkyl(C_{1-4});

R^3 is a C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or $(CH_2)_k$ aryl group (k=1-4), and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, OCF_3, SMe, $COOR^7$, $SO_2NR^5R^6$, SO_3R^7, CO-lower alkyl, SCF_3 CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl,

aryl, and aryloxy wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, or aryloxy groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, $NHCOCH_3$, OCF3, SMe, $COOR^7$, SO_3R^7, $SO_2NR^5R^6$, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl;

R^4 is a C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, OCF_3, SMe, $COOR^7$, $SO_2NR^5R^6$, SO_3R^7, CO-lower alkyl, SCF_3 CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, and aryloxy wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, or aryloxy groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, $NHCOCH_3$, OCF3, SMe, $COOR^7$, SO_3R^7, $SO_2NR^5R^6$, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl;

R^5 and R^6 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH_2 aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^7R^8$, NR^7R^8, $NHCOCH_3$, OCF_3, SMe, $COOR^9$, SO_3R^7, $SO_2NR^7R^8$, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, or aryl groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^8R^9$, NR^8R^9, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl,

or R^5 and R^6 may form part of a 5, 6 or 7 membered cyclic structure which may be either saturated or unsaturated and that may contain up to four heteroatoms selected from O, N or S and said cyclic structure may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, Me, NO_2, OH, OMe, OEt, OCF_3, SMe, $COOR^7$,

$SO_2NR^8R^9$, SO_3R^7, $NHCOCH_3$, COEt, COMe, or halogen;

R^7 may be independently selected from H or C_{1-6} alkyl;

R^8 and R^9 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH_2 aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from halogen, CF_3, OCF3, OEt, CCl_3, Me, NO_2, OH, OMe, SMe, COMe, CN, $COOR^7$, SO_3R^7, COEt, $NHCOCH_3$, or aryl;

an aryl moiety can be a 5 or 6 membered aromatic heterocyclic ring (containing up to 4 hetero atoms independently selected from N, O, or S) or a 6 membered aromatic non-heterocyclic ring or a polycycle;

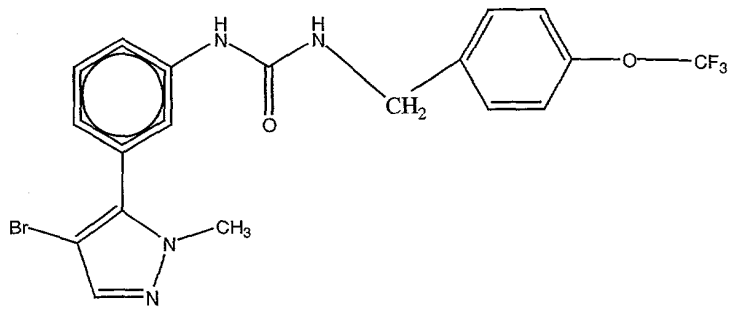
C_{1-6} alkyl moieties can be straight chain or branched;

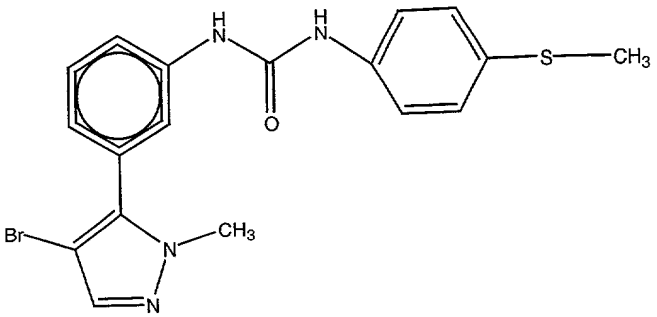
optionally substituted C_{1-6} alkyl moieties can be straight chain or branched;

C_{2-6} alkenyl moieties can be straight chain or branched; and

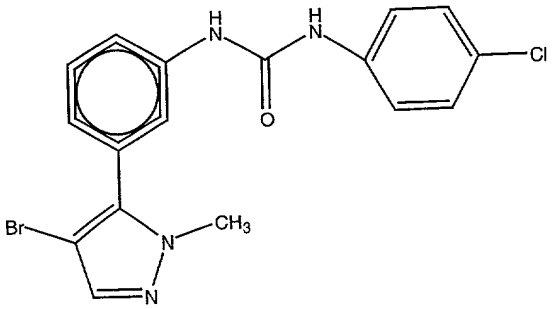
optionally substituted C_{2-6} alkenyl moieties can be straight chain or branched.

21. **(New)** A compound having a structure selected from the group consisting of:

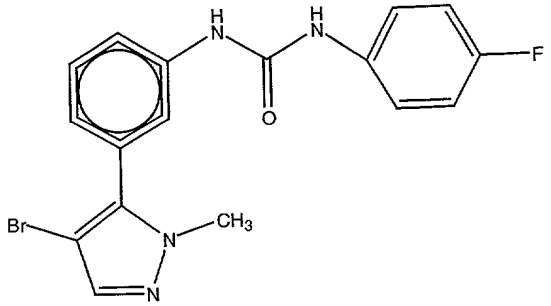



H
N
H
N
O
S
CH3
Br
N
CH3
N

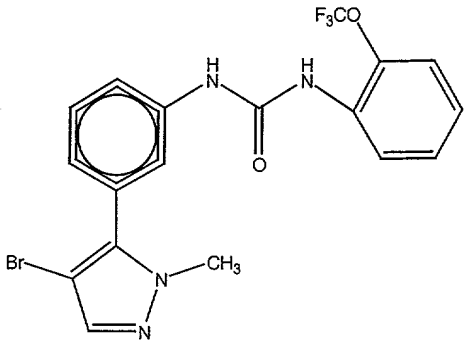
,


H
N
H
N
O
Cl
Br
N
CH3
N

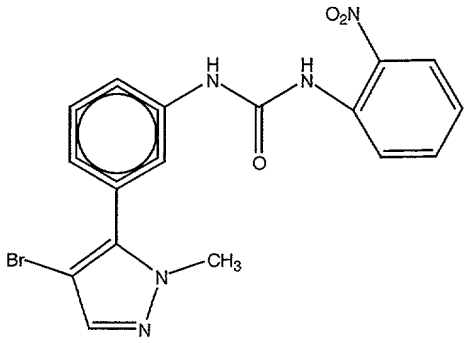
,


H
N
H
N
O
F
Br
N
CH3
N

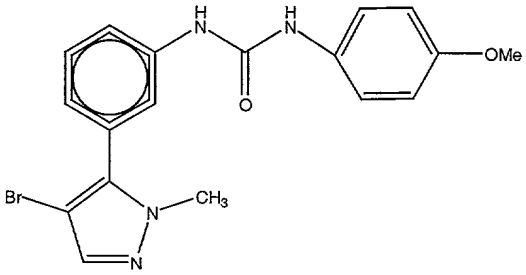
,


F3CO
H
N
H
N
O
Br
N
CH3
N

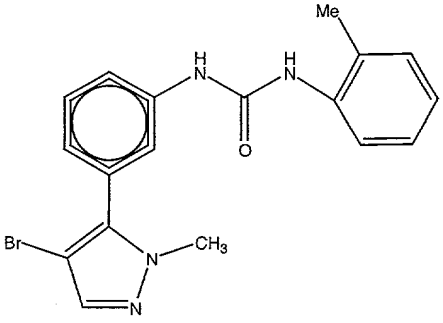
,


O2N
H
N
H
N
O
Br
N
CH3
N

,


H
N
H
N
OMe
O
Br
N
CH3
N

,


Me
H
N
H
N
O
Br
N
CH3
N

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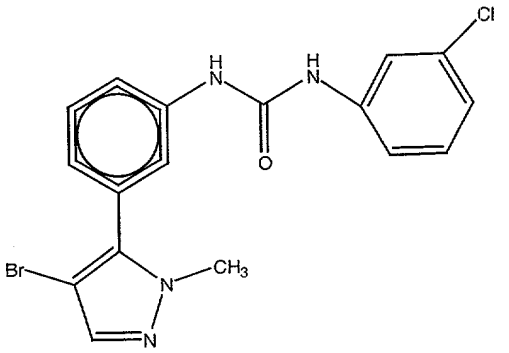

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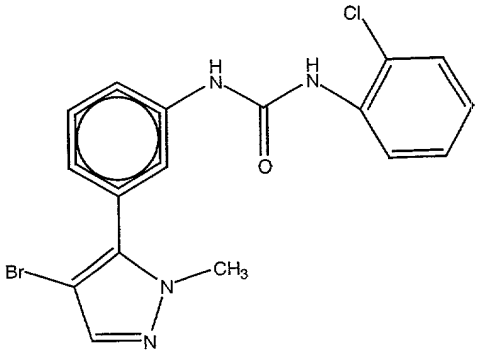

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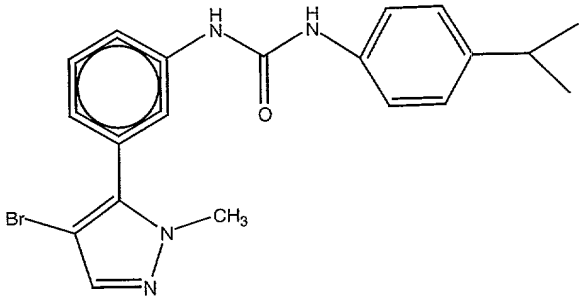

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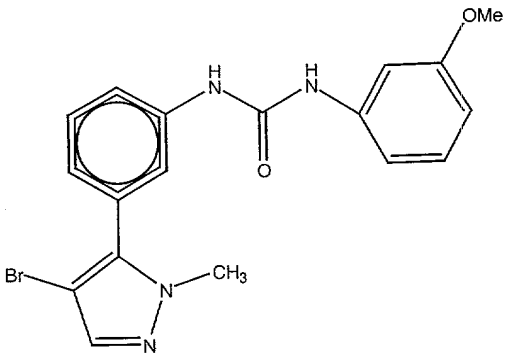

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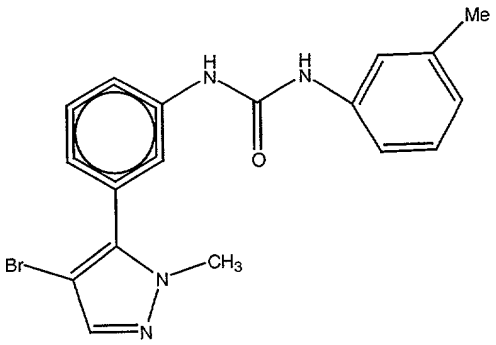
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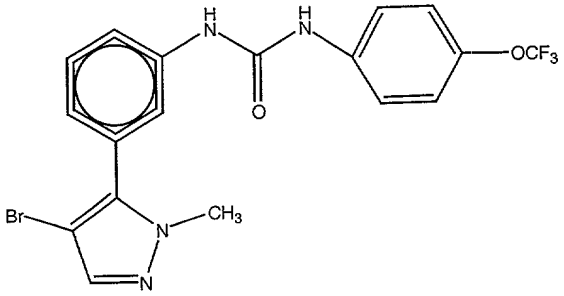
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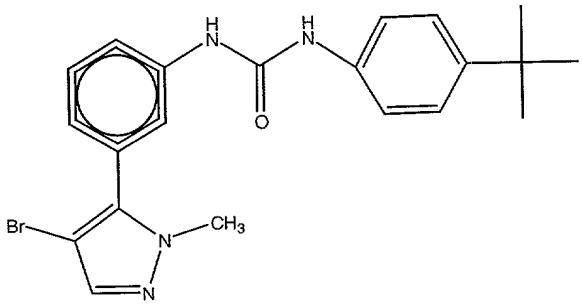
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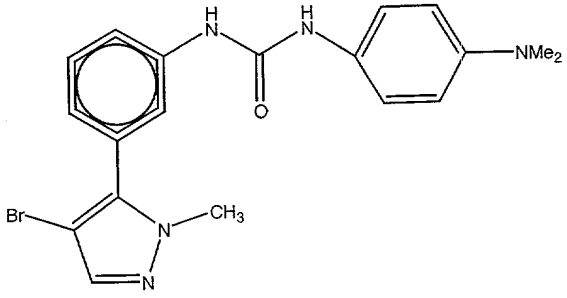
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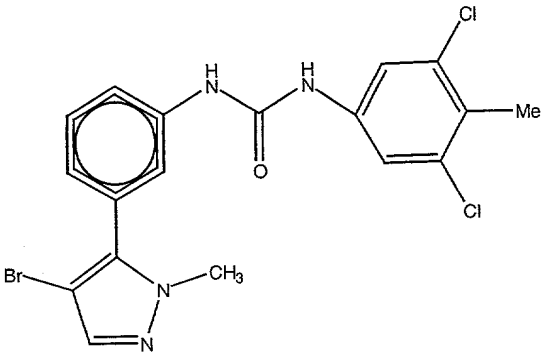
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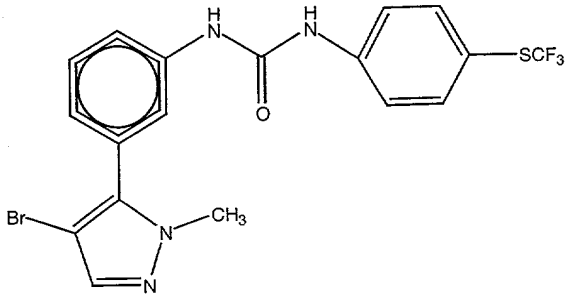
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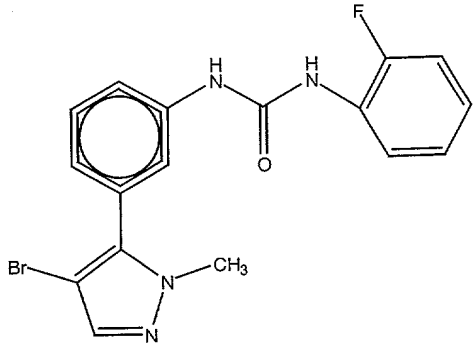
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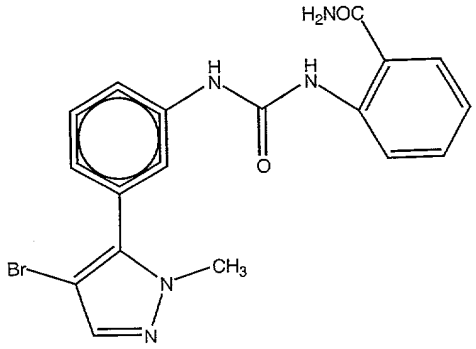
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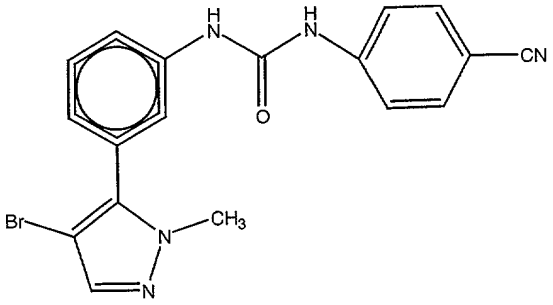

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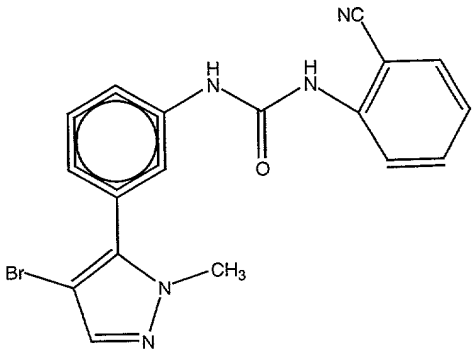

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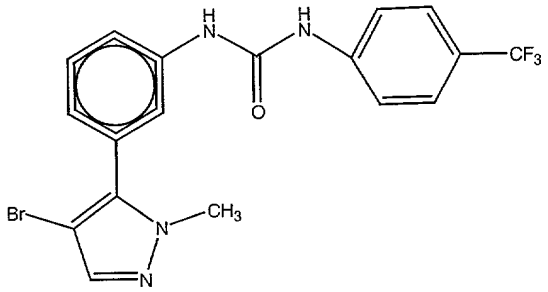

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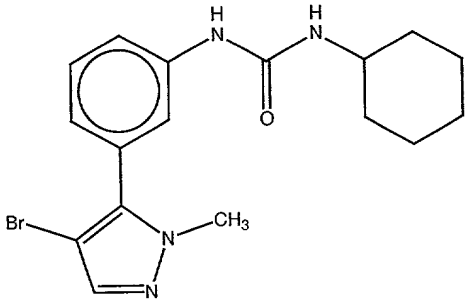

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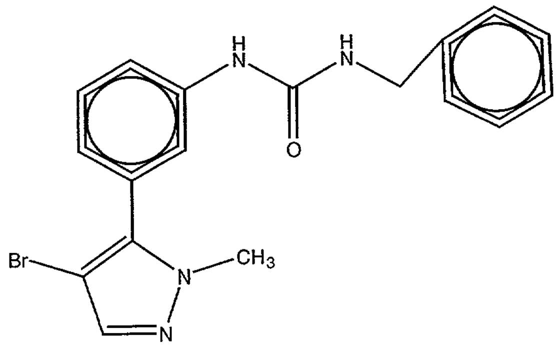
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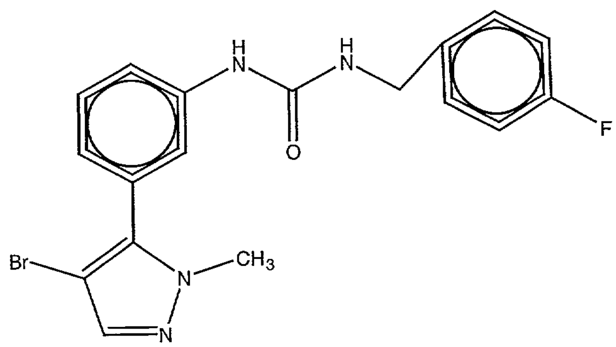
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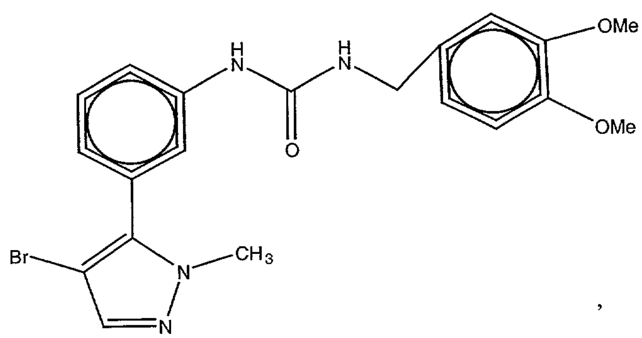
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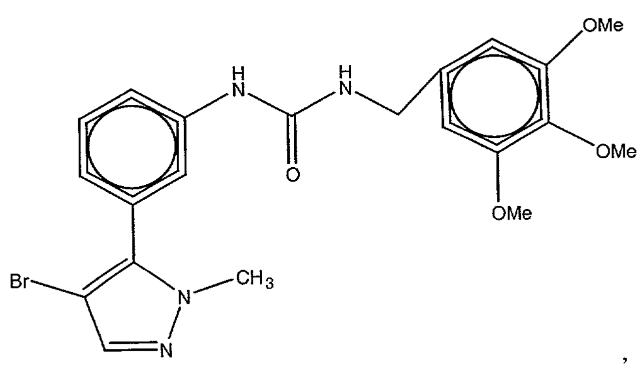
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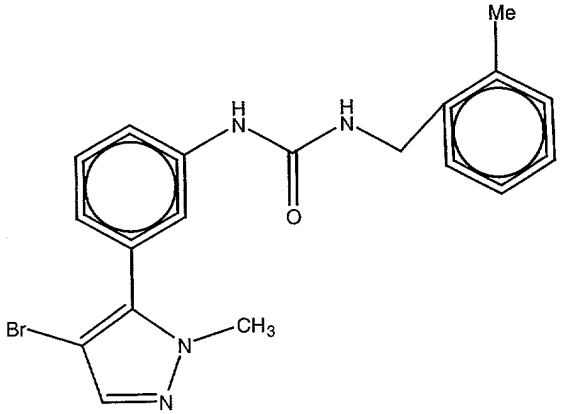
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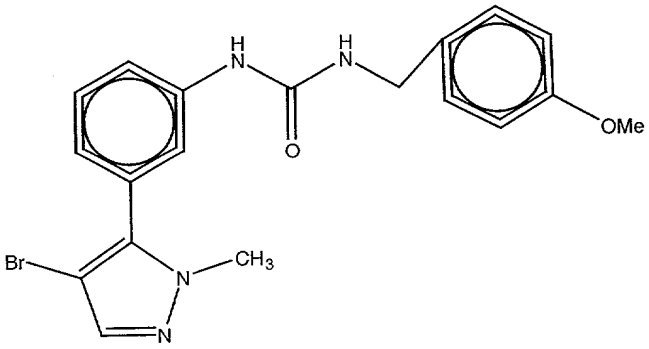
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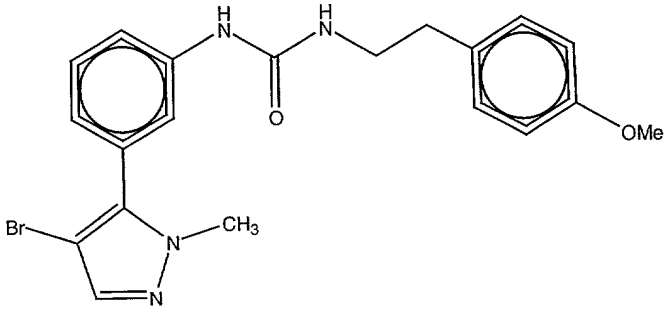
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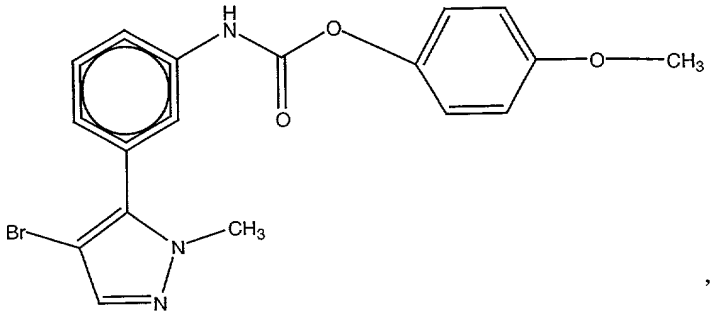
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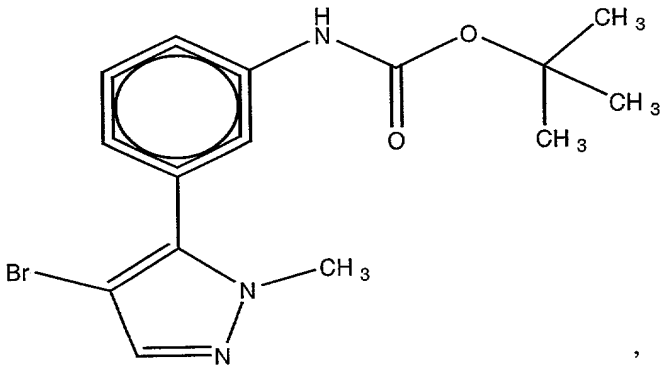

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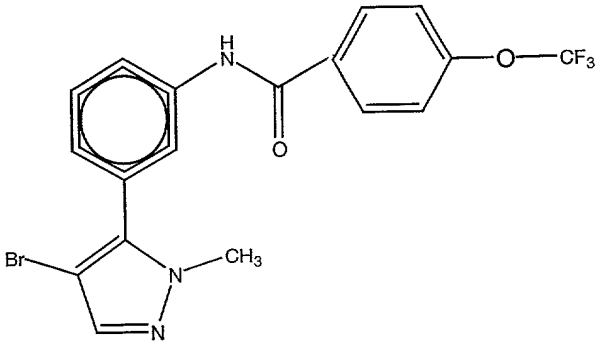

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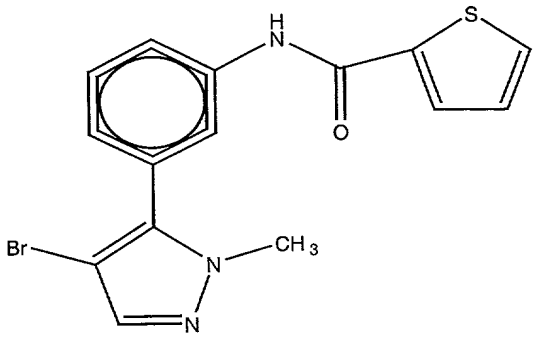

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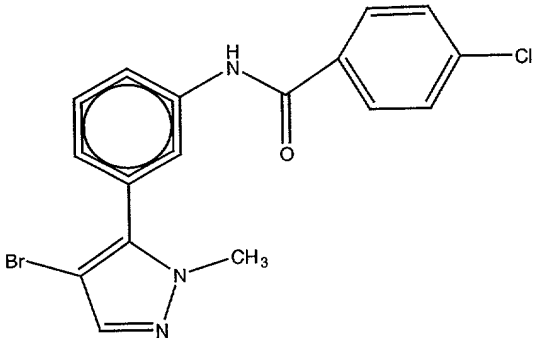
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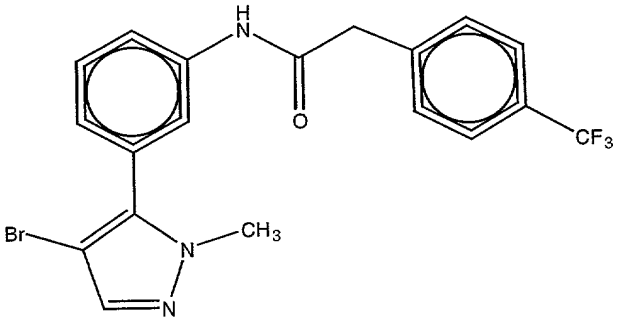
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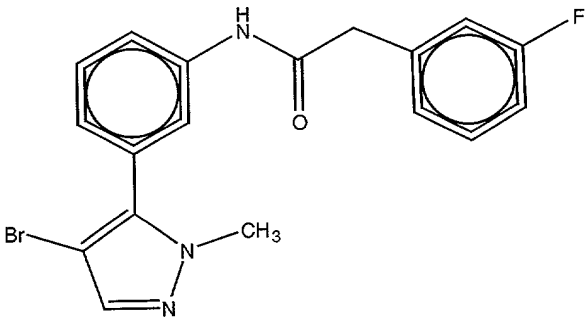
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CH3
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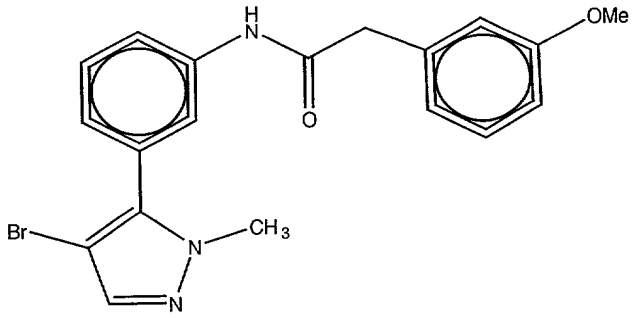
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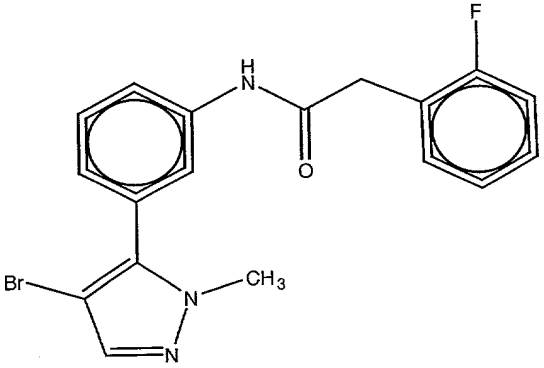
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Br
N
CH3
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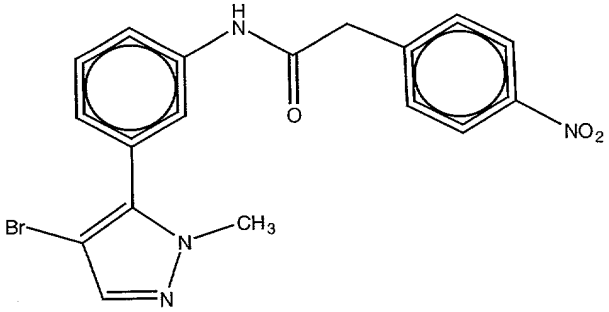
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NO2
Br
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CH3
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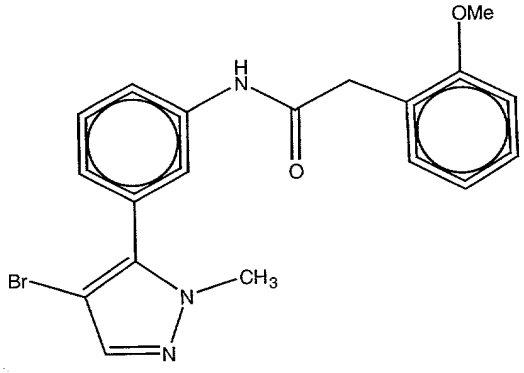
, or


OMe
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Br
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CH3
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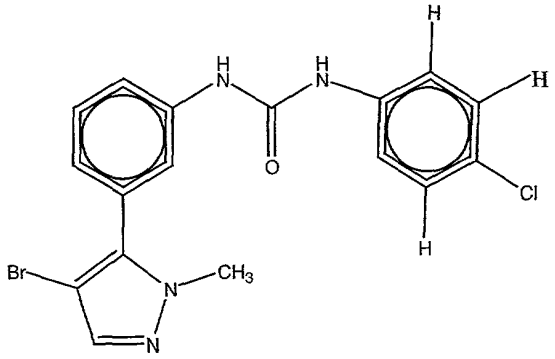
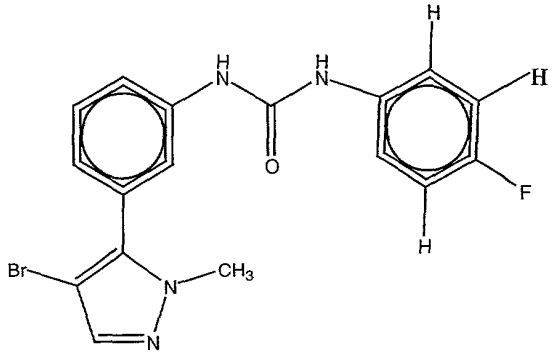
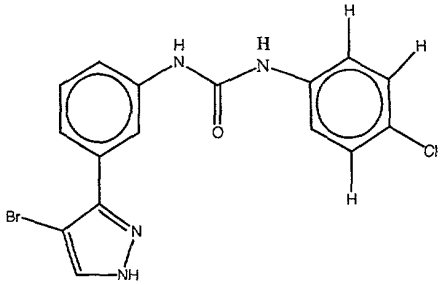
22. **(New)** A compound structurally represented as follows:



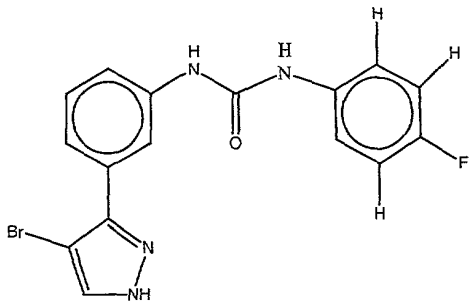
23. **(New)** A compound structurally represented as follows:



24. **(New)** A compound structurally represented as follows:



25. **(New)** A compound structurally represented as follows:



26 **(New)** A composition comprising a compound of any one of claims 21-25.

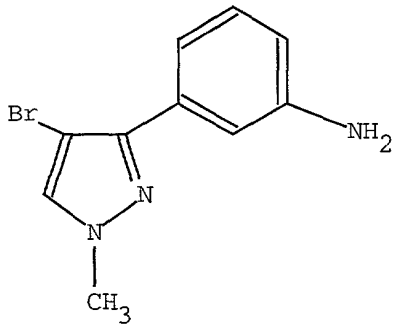
REMARKS

Claim 1 was pending. Claim 1 has been cancelled without prejudice. New claims 14-26 have been added. No new matter has been added.

Upon entry of this amendment, claims 14-26 will be pending.

This is a continuation of U.S. Ser. No. 09/292,072, filed April 14, 1999, ("the 072 application"), which is presently pending. In this preliminary amendment, Applicants correct a nomenclature error in the parent application. This error arose from a mistaken structure assigned to a synthetic precursor. The synthetic precursor was purchased by Applicants from Maybridge

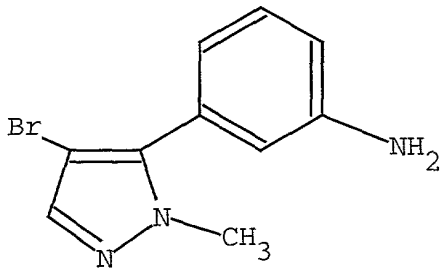
Chemical Company (Maybridge plc) under the designation KM 01978, and was said by Maybridge plc to be have the structure:



KM 01978

The compound was named by Maybridge plc 3-(4-bromo-1-methylpyrazole-3-yl)phenylamine. This was reported in the parent application at page 31, lines 2-7. Each of the compounds synthesized and characterized by Applicants, as reported in the 072 application in Example 13, Experiments 2-43, were prepared according to the synthetic procedures reported in the 072 application, using this starting material.

Recently, Applicants discovered that the compound provided to Applicants as KM 01978 in fact has the structure:



i.e., 3-(4-bromo-2-methylpyrazole-3-yl)phenylamine, which differs from the structure assigned by Maybridge plc in that the pyrazole methyl group is located on the adjacent nitrogen atom of the pyrazole ring. Accordingly, the name of each compound made and characterized by

Applicants, and deriving from the 3-(4-bromo-2-methylpyrazole-3-yl)phenylamine starting material, has been corrected. It is believed that no new matter is introduced by the correction, as the changes merely provide the accurate name of the compounds that Applicants prepared and characterized as described in the parent application. In addition, the generic formulae disclosed by Applicants also have been corrected. Inasmuch as those formuae were clearly based on the compounds prepared by Applicants in Example 13, Experiments 2-43, it is believed that the change to the generic structures also does not constitute new matter.

In addition, the specification has been amended to provide the correct structure and name of the Maybridge starting material, and compounds deriving therefrom, as discussed above.

Applicants present herein new claims 14 to 26. Claims 14 to 26 find support in the specification at, *inter alia*, page 31, line 8 to page 37, line 9; page 39; page 40; page 41; page 42; page 43; page 44, page 45; pages 47-49; page 51; pages 52-54; and pages 66-73.

Applicants attach hereto a paper and CRF version of the most recent Sequence Listing filed in the present application's parent.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Applicants respectfully request that this amendment be entered without prejudice.

Applicants believe all of the claims presently before the Examiner patentably define the invention over the prior art and are otherwise in condition for ready allowance. Applicants respectfully request early notification of the same.

Respectfully submitted,

Gwilym J.O. Attwell
Registration No. 45,449

Michael P. Straher, Ph.D.
Registration No. 38,325

Date: January 23, 2002
WOODCOCK WASHBURN LLP
One Liberty Place - 46th Floor
Philadelphia, PA 19103
(215) 568-3100

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Sequence Listing:

Please delete the Sequence Listing on file and insert therefore pages **1-19** comprising the most recently filed Sequence Listing.

In the Specification:

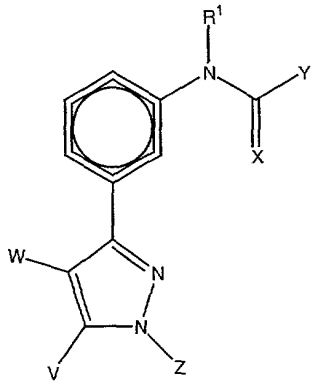
Please amend the paragraph on page 31, lines 2 to 7, as follows:

Based upon these results, structure activity analysis of the 103487 compound suggested that a series of derivatives of N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][{(4-trifluoromethoxy)phenyl}aminocarboxamide [3-(4-bromo-1-methylpyrazole-3-yl)phenylamine] would exhibit similar 5-HT_{2A} activity and selectivity. A series of derivatives of N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][{(4-trifluoromethoxy)phenyl}aminocarboxamide [3-(4-bromo-1-methylpyrazole-3-yl)phenylamine] were synthesized. These "directed" library compounds (Tripos, Inc.) were then analyzed in accordance with the protocols of Examples 9c(1), 9c(2) and 9d.

Please amend the paragraph on page 31, lines 8 to 12, as follows:

This series of compounds exhibits highly selective 5-HT2A activity. Accordingly, in the first aspect of the invention, a series of compounds exhibiting 5-HT_{2A} receptor activity that are useful as inverse agonists at such receptors is designated by the general formula (A):

[



(A)

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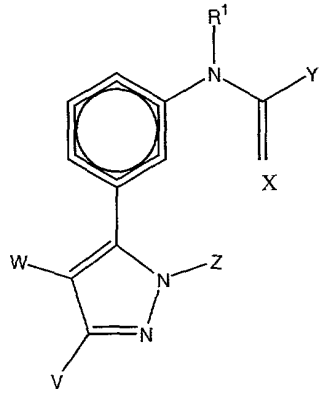

(A)

(A)

Please amend the paragraph on page 34, line 1, as follows:

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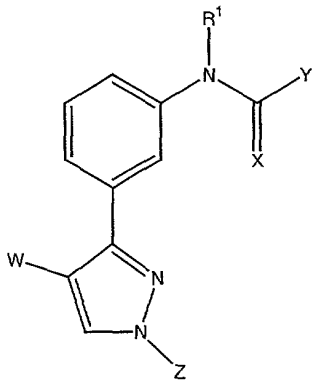

(B)

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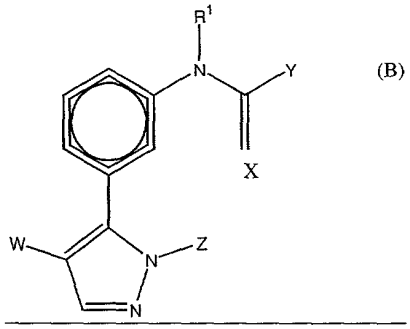

(B)

Please amend the paragraph on page 36, lines 9-10, as follows:

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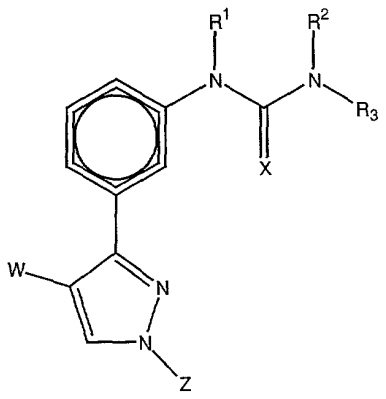

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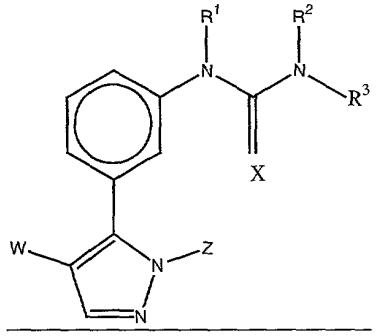
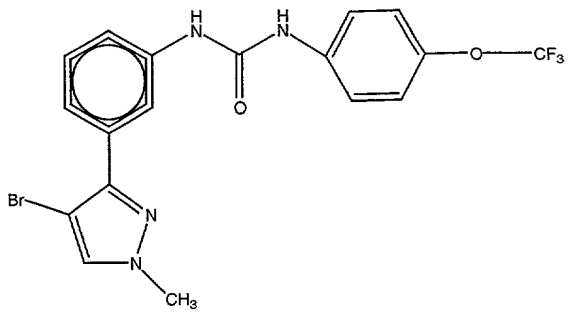


Please amend the paragraph on page 37, lines 3-4, as follows:

[



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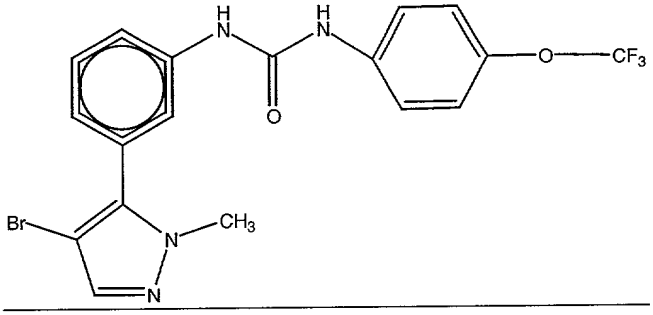
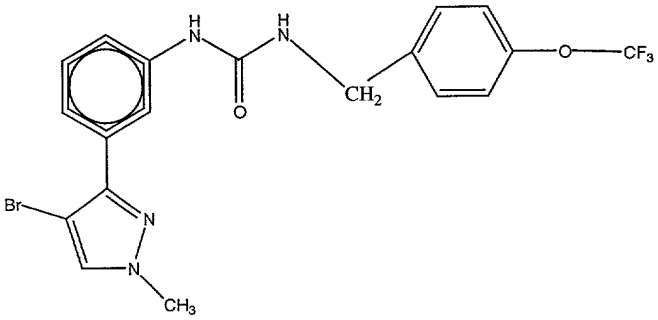


Please amend the paragraph on page 37, lines 8-9, as follows:

[



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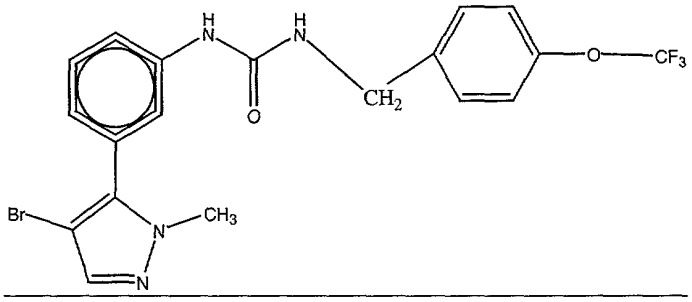
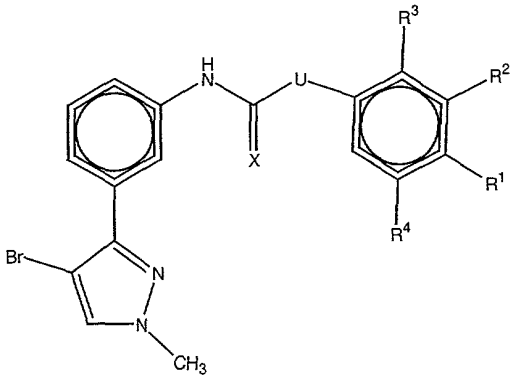


Please amend the paragraph on page 39, lines 1-2, as follows:

[



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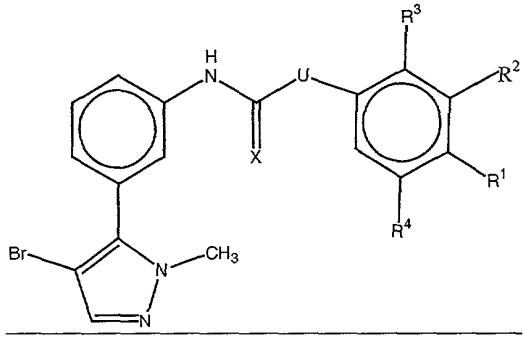


Please amend the paragraphs spanning pages 39 to page 41 as follows:

Compound No.	R^1	R^2	R^3	R^4	X	U	IP_3 % of Control	IP_3 AP-3 IC_{50} nM	WT $5HT_{2A}$ LSD IC_{50} nM
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][(4-methylthiophenyl)amino]carboxamide [N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl][(4-methylthiophenyl)amino]carboxamide]									
116079	SCH_3	H	H	H	O	NH	16	17	4
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][(4-chlorophenyl)amino]carboxamide [N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl][(4-chlorophenyl)amino]carboxamide]									
116081	Cl	H	H	H	O	NH	10	3.2	11
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-(4-fluorophenyl)carboxamide [{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-amino}-N-(4-fluorophenyl)carboxamide]									
116082	F	H	H	H	O	NH	11	-	7

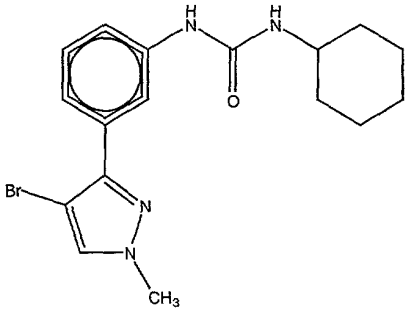
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-[2-(trifluoromethoxy)phenyl]carboxamide [{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-amino}-N-[2-(trifluoromethoxy)phenyl]carboxamide]									
116087	H	H	CF_3O	H	O	NH	11	-	200
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-(2-nitrophenyl)carboxamide [{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-amino}-N-(2-nitrophenyl)carboxamide]									
116089	H	H	NO_2	H	O	NH	27	-	238
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-(4-methoxyphenyl)carboxamide [{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-amino}-N-(4-methoxyphenyl)carboxamide]									
116091	MeO	H	H	H	O	NH	12	-	19
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(2-methylphenyl)carboxamide [{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(2-methylphenyl)carboxamide]									
116092	H	H	Me	H	O	NH	32	-	131
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-[4-(trifluoromethyl)phenyl]carboxamide [{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-amino}-N-[4-(trifluoromethyl)phenyl]carboxamide]									
116097	CF_3	H	H	H	O	NH	11	-	65

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-(3-chlorophenyl)carboxamide [{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-amino}-N-(3-chlorophenyl)carboxamide]									
116105	H	Cl	H	H	O	NH	11	-	39
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-[2-chlorophenyl)carboxamide [{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-amino}-N-[2-chlorophenyl)carboxamide]									
116108	H	H	Cl	H	O	NH	6	-	249
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-[4-(methylethyl)phenyl]carboxamide [{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-[4-(methylethyl)phenyl]carboxamide]									
116110	isopropyl	H	H	H	O	NH	7	-	338
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-(3-methoxyphenyl)carboxamide [{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-amino}-N-(3-methoxyphenyl)carboxamide]									
116111	H	MeO	H	H	O	NH	7	-	106
[{3-(4-bromo-2-methylpyrazol-3-yl)phenyl}-amino]-N-(3-methylphenyl)carboxamide [[{3-(4-bromo-1-methylpyrazol-3-yl)phenyl}-amino]-N-(3-methylphenyl)carboxamide]									
116112	H	Me	H	H	O	NH	14	-	57

[{3-(4-bromo-2-methylpyrazol-3-yl)phenyl}-amino]-N-methyl-N-[4-(trifluoromethoxy)phenyl]carboxamide [[{3-(4-bromo-1-methylpyrazol-3-yl)phenyl}-amino]-N-methyl-N-[4-(trifluoromethoxy)phenyl]carboxamide]									
116113	CF_3O	H	H	H	O	NCH_3	-	193	2
N-[4-(tert-butyl)phenyl]{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}carboxamide [N-[4-(tert-butyl)phenyl]{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}carboxamide]									
116119	t-butyl	H	H	H	O	NH	17	-	476
N-[4-(dimethylamino)phenyl]{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}carboxamide [N-[4-(dimethylamino)phenyl]{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}carboxamide]									
116122	NMe_2	H	H	H	O	NH	9	-	309
N-(3,5-dichloro-4-methylphenyl){[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}carboxamide [N-(3,5-dichloro-4-methylphenyl){[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}carboxamide]									
116138	Me	Cl	H	Cl	O	NH	23	-	122

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-[4-(trifluoromethylthio)phenyl]carboxamide [{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-amino}-N-[4-(trifluoromethylthio)phenyl]carboxamide]									
116139	CF_3S	H	H	H	O	NH	12	-	56
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-(2-fluorophenyl)carboxamide [{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-amino}-N-(2-fluorophenyl)carboxamide]									
116144	H	H	F	H	O	NH	12	-	37
2-({[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}carbonylamino)benzamide [2-({[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-amino}carbonylamino)benzamide]									
116145	H	H	$CONH_2$	H	O	NH	31	-	7473
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-(4-cyanophenyl)carboxamide [{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-amino}-N-(4-cyanophenyl)carboxamide]									
116147	CN	H	H	H	O	NH	12	-	2
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}-N-(2-cyanophenyl)carboxamide [{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-amino}-N-(2-cyanophenyl)carboxamide]									
116148	H	H	CN	H	O	NH	30	-	348

[



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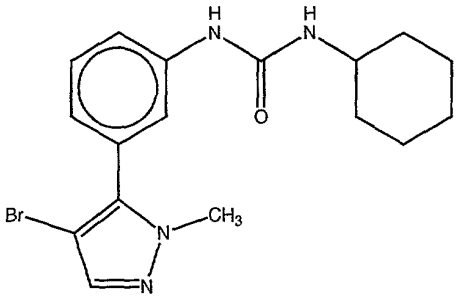


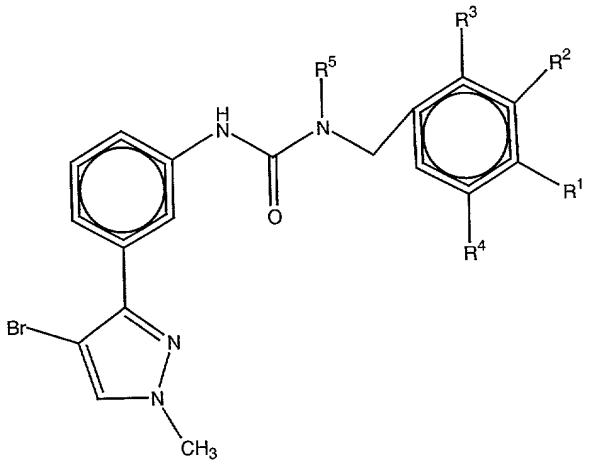
Please amend the table on page 42 as follows:

Compound No.		IP_3 AP-3 IC_{50} nM	WT $5HT_{2A}$ LSD IC_{50} nM

116141	N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-[cyclohexylamino]carboxamide [N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-[cyclohexylamino]carboxamide]	114	81

Please amend the paragraph on page 42, lines 3-4, as follows:

[



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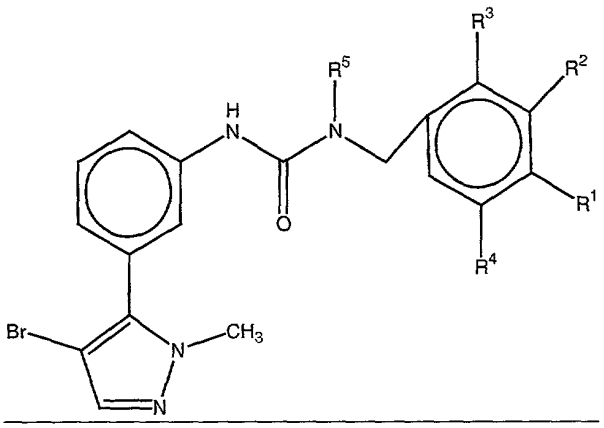


Please amend the table on page 42, lower, to 43, upper, as follows:

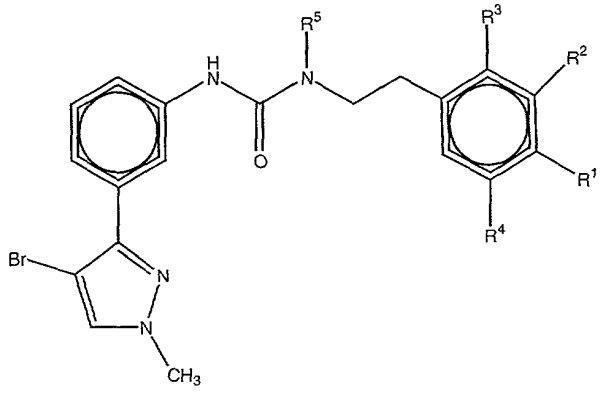
Compound No.	R^1	R^2	R^3	R^4	R^5	IP_3 AP-3 IC_{50} nM	WT $5HT_{2A}$ LSD IC_{50} nM
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-[phenylmethylamino]carboxamide [N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-[phenylmethylamino]carboxamide]							
116143	H	H	H	H	H	120	47

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-[{(4-fluorophenyl)methyl}amino]carboxamide [N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-[{(4-fluorophenyl)methyl}amino]carboxamide]							
116182	F	H	H	H	H	89	132
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]- [{(3,4-dimethoxyphenyl)methyl}amino]-carboxamide [N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]- [{(3,4-dimethoxyphenyl)methyl}amino]-carboxamide]							
116183	OMe	OMe	H	H	H	-	1010
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-[{(3,4,5-trimethoxyphenyl)methyl}amino]-carboxamide [N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-[{(3,4,5-trimethoxyphenyl)methyl}amino]-carboxamide]							
116184	OMe	OMe	H	OMe	H	-	2960
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][{(2-methylphenyl)methyl}amino]carboxamide [N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl][{(2-methylphenyl)methyl}amino]carboxamide]							
116185	H	H	Me	H	H	-	769

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][{(4-methoxyphenyl)methyl}amino]carboxamide [N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl][{(4-methoxyphenyl)methyl}amino]carboxamide]							
116189	OMe	H	H	H	H	-	102

Please amend the paragraphs on pages 43-44, as follows:

[



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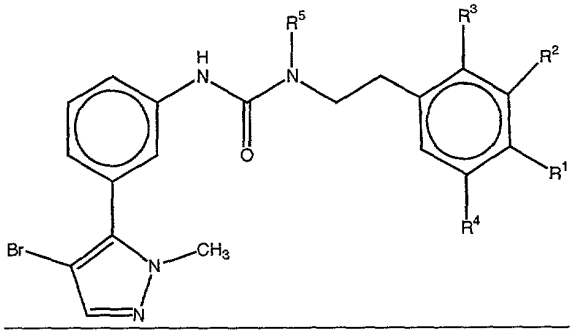
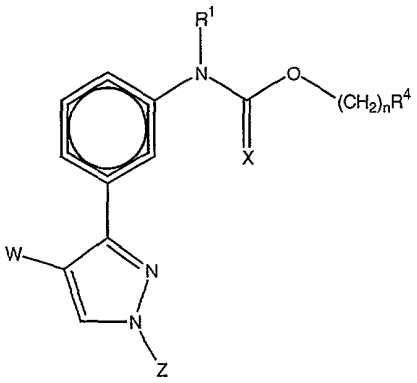


Compound No.	R^1	R^2	R^3	R^4	R^5	IP_3 AP-3 IC_{50} nM	WT $5HT_{2A}$ LSD IC_{50} nM
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][{2-(4-methoxyphenyl)ethyl}amino]carboxamide [N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl][{2-(4-methoxyphenyl)ethyl}amino]carboxamide]							
116194	OMe	H	H	H	H	32	61

Please amend the paragraph on page 44, lines 7-8, as follows:

[



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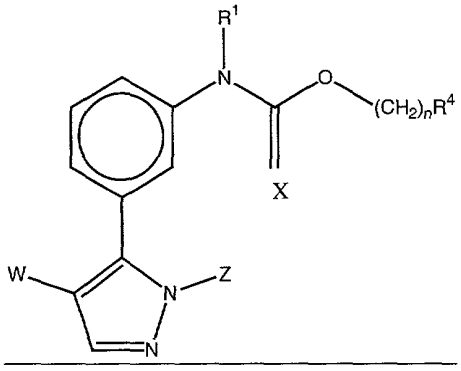
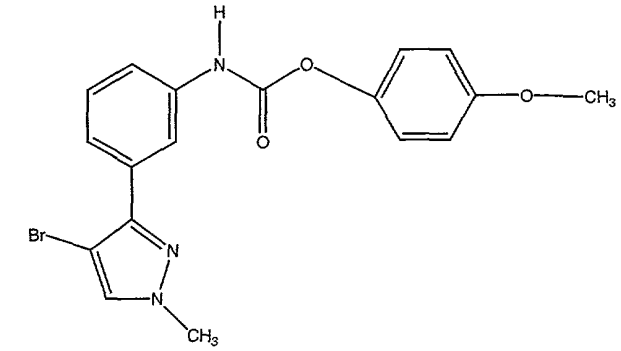


Please amend the paragraph on page 44, line 17, to page 45, line 2, as follows:

116100

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][4-methoxyphenoxy]carboxamide
[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl][4-methoxyphenoxy]carboxamide]

[



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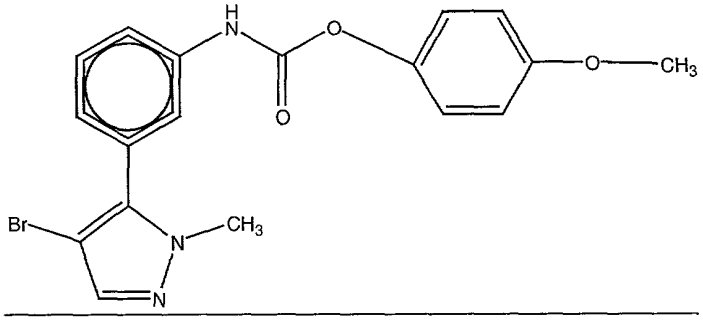


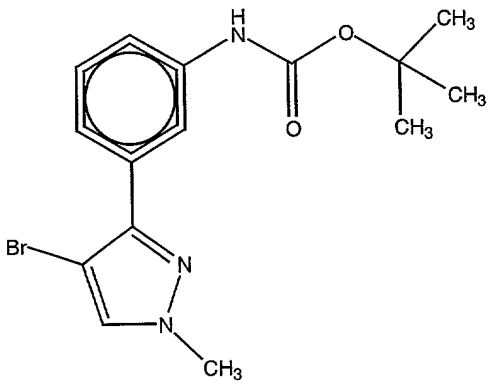
Please amend the paragraph on page 45, lines 6-7 as follows:

116192

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(1,1-dimethylethoxy)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(1,1-dimethylethoxy)carboxamide]

[



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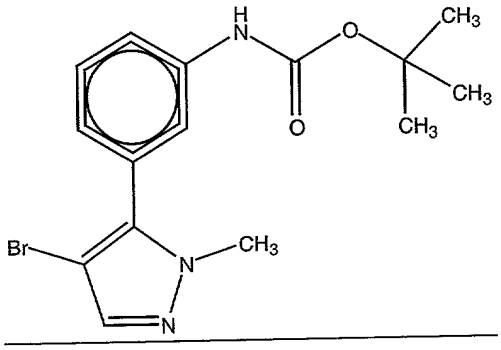
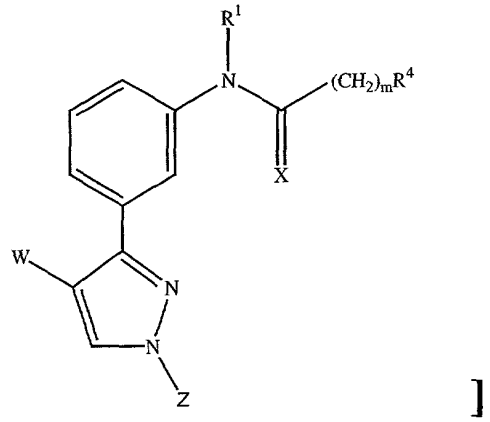


Please amend the paragraph on page 47, lines 3-4 as follows:

[



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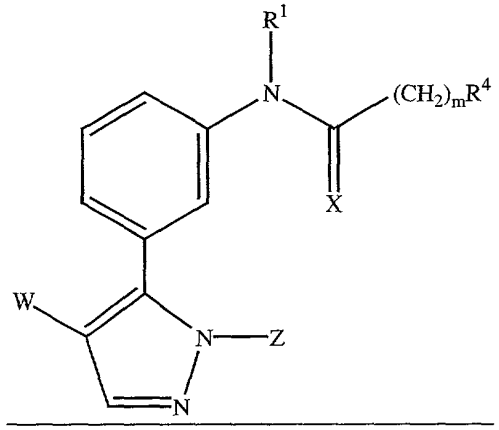


Please amend page 47, line 13, to page 49, line 1 as follows:

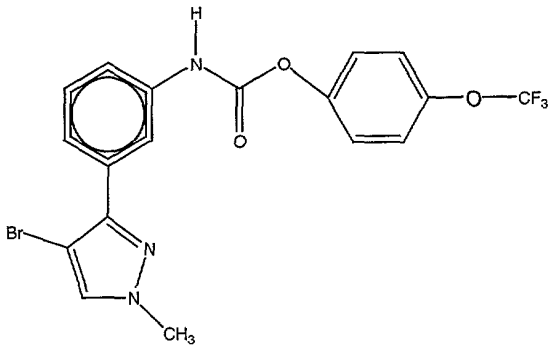
116101

m = 0, R^1 = H, R^4 = 4-trifluoromethoxyphenyl

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl][4-trifluoromethoxyphenyl]carboxamide]

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][4-trifluoromethoxyphenyl]carboxamide

[



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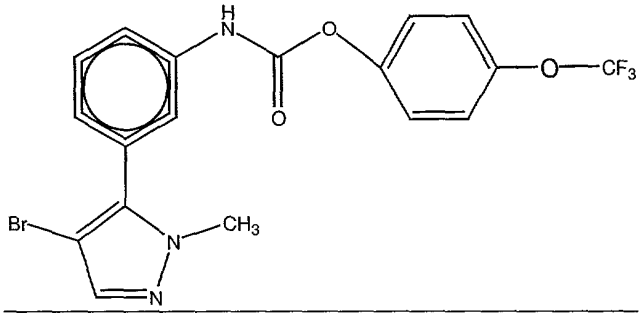


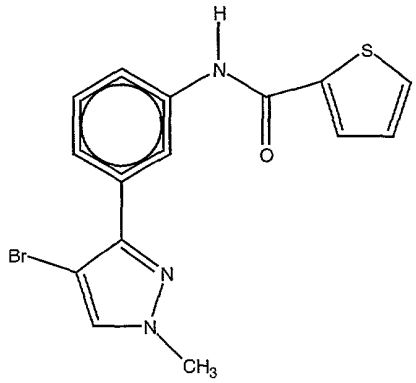
116102

m=0, R^1= H, R^4= thiophene

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][2-thienyl]carboxamide

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl][2-thienyl]carboxamide]

[



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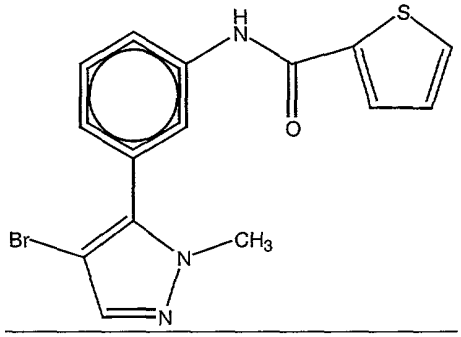


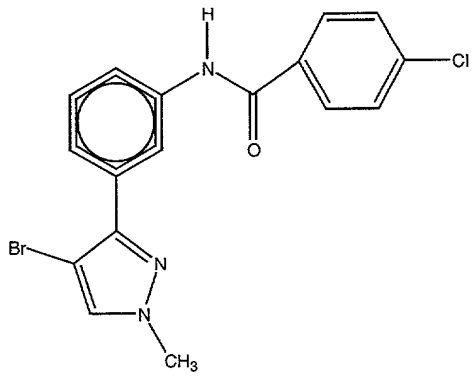
116120

m=0, R^1= H, R^4= chlorophenyl

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][4-chloro-phenyl]carboxamide

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl][4-chloro-phenyl]carboxamide]

[



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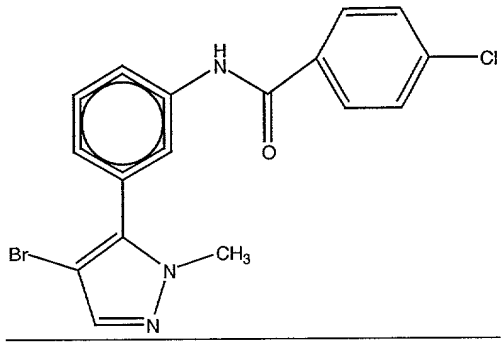
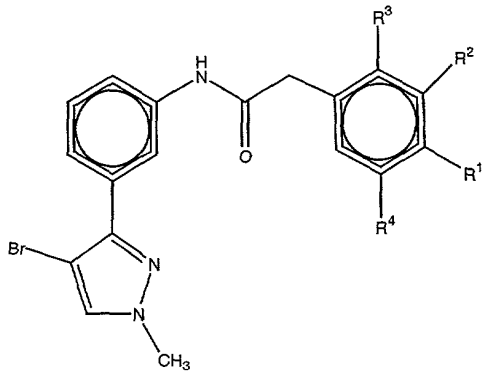


Please amend page 51, line 6, to page 52, line 1 as follows:

[



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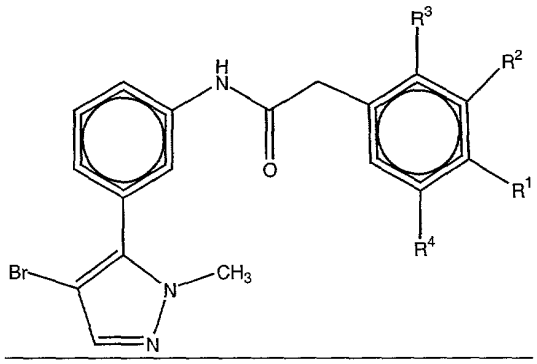


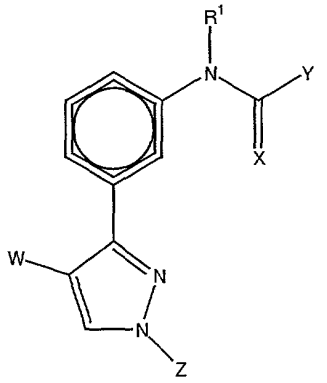
Name	Compound No.	R^1	R^2	R^3	R^4	IP_3 IC_{50} nM	LSD IC_{50} nM
[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-2-[4-(trifluoromethoxy)-phenyl]acetamide] N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-[4-(trifluoromethoxy)-phenyl]acetamide	116137	OCF_3	H	H	H	-	106

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-2-(3-fluorophenyl)acetamide] N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(3-fluorophenyl)acetamide	116174	H	F	H	H	153	318
[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-2-(3-methoxyphenyl)acetamide] N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(3-methoxyphenyl)acetamide	116175	H	OMe	H	H	108	625
[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-2-(2-fluorophenyl)acetamide] N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(2-fluorophenyl)acetamide	116176	H	H	F	H	129	662
[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-2-(4-nitrophenyl)acetamide] N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(4-nitrophenyl)acetamide	116177	NO_2	H	H	H	61	108
N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(2-methoxyphenyl)acetamide	116178	H	H	OMe	H	165	2300

[compound names not provided]

Please amend the paragraph on page 52, line 7 as follows:

[



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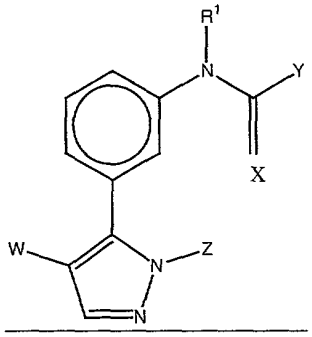
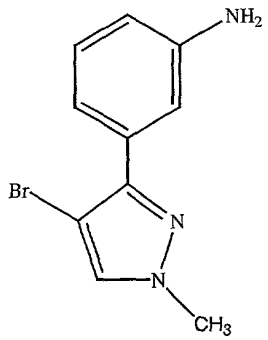


Please amend the paragraph on page 55, lines 5-13, as follows:

Compounds of general formula **(I)** can be obtained *via* a variety of synthetic routes all of which would be familiar to one skilled in the art. The reaction of isocyanates with amines is a commonly practiced method for the formation of ureas (see Org. Syn. Coll. Vol. V, (1973), 555). Amine (IV), 3-(4-bromo-2-methylpyrazole-3-yl)phenylamine [3-(4-bromo-1-methylpyrazole-3-yl)phenylamine], commercially available from Maybridge Chemical Company, Catalog No. KM01978, CAS No. 175201-77-1) reacts readily with isocyanates **(V)** in inert solvents such as halocarbons to yield the desired ureas of general formula **(I)** wherein $R^1 = R^2 = H$:

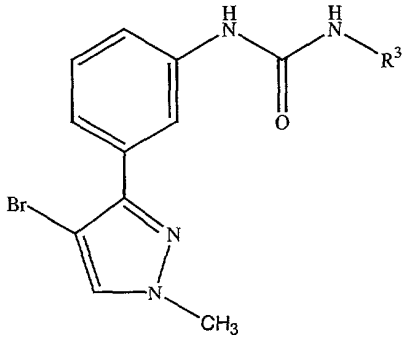
[



(IV)

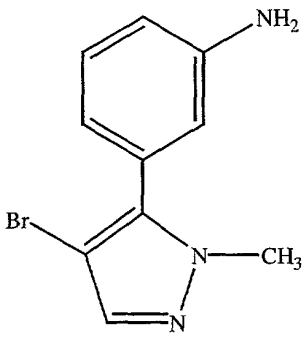
+ OCN—R^3 ⟶

(V)



(I) $R^1 = R^2 = H$

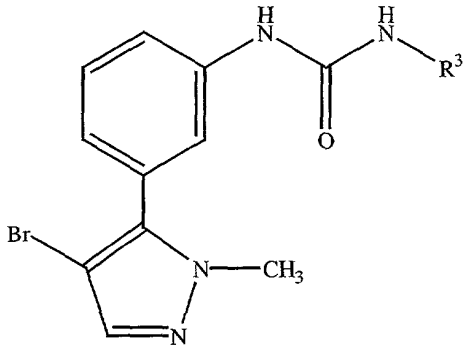
]



(IV)

+ OCN—R^3 ⟶

(V)



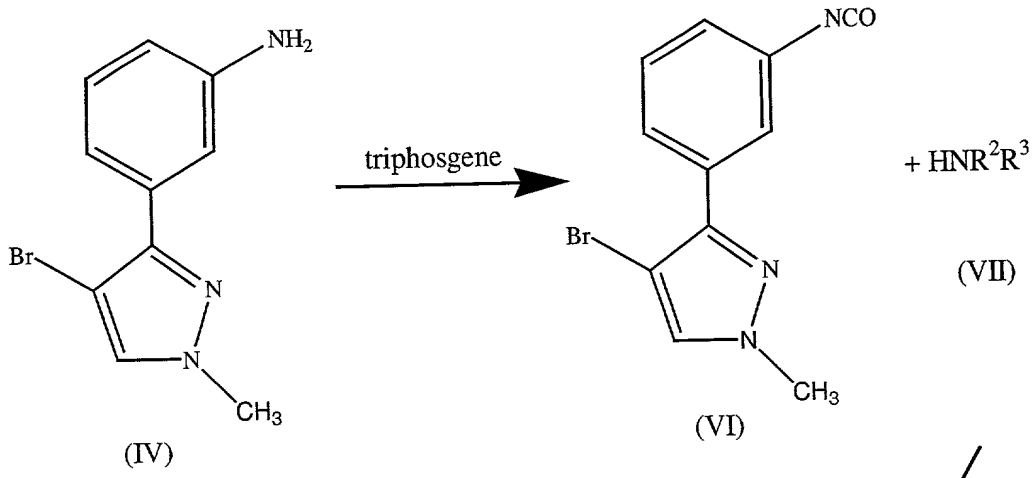
(I) $R^1 = R^2 = H$

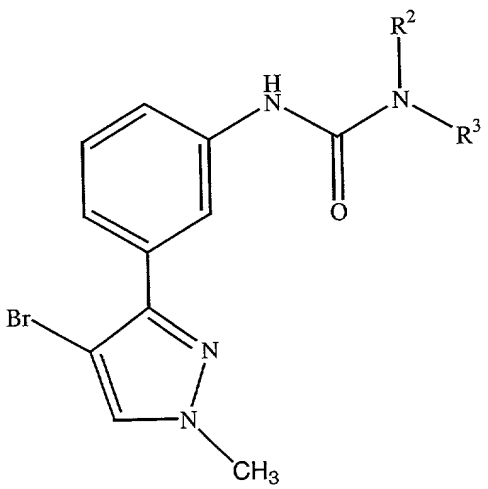
Please amend the paragraph spanning page 55, line 14, to page 56, line 1, as follows:

Alternatively the amine **(IV)** can be converted to the corresponding isocyanate **(VI)** by the action of phosgene or a suitable phosgene equivalent, *e.g.* triphosgene, in an inert

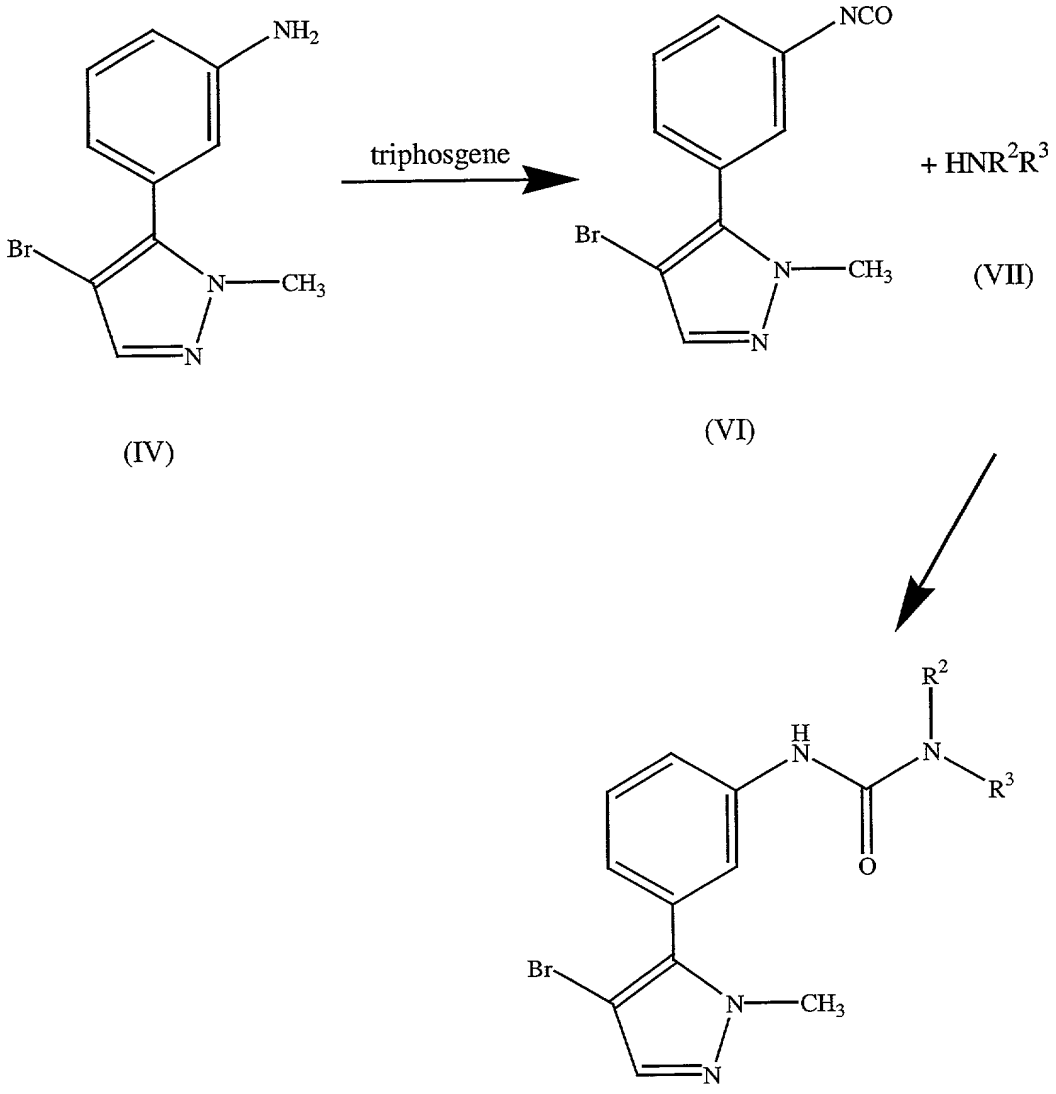
solvent such as a halocarbon in the presence of an organic base such as triethylamine or ethyldiisopropylamine. Isocyanate **(VI)** reacts with amines of general formula **(VII)**, in an analogous fashion to that described above for the reaction of **(IV)** with **(V)**, yielding the desired ureas of general formula **(I)** wherein R^1 = H:

[


NH2
triphosgene
NCO
+ HNR2R3
Br
N
N
CH3
(IV)
(VI)
(VII)


R2
H
N
N
R3
O
Br
N
N
CH3

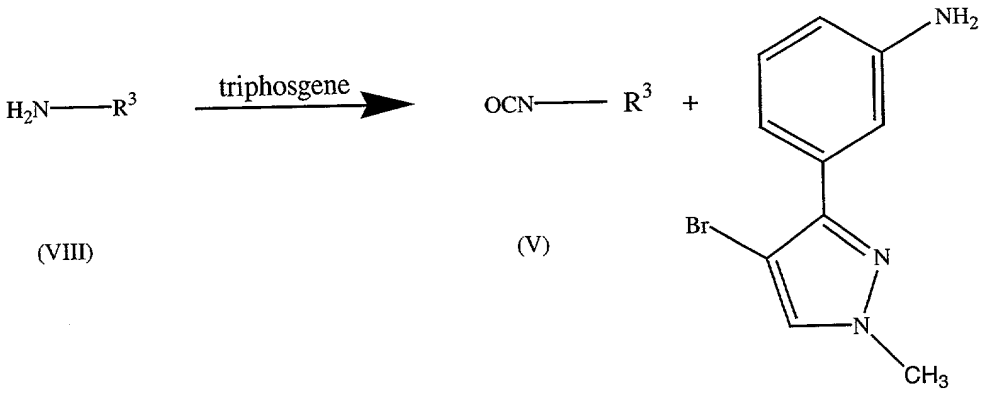
(I) $R^1 = H$]



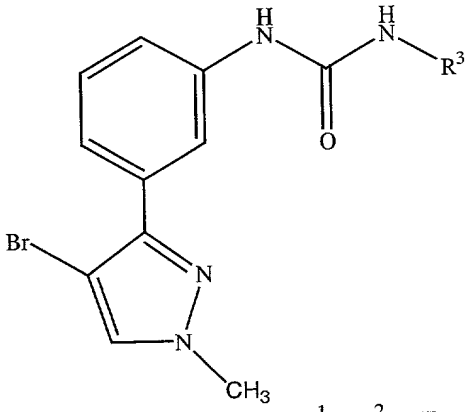
Please amend the paragraph spanning page 56, line 2, to page 57, line 1, as follows:

Alternatively wherein the isocyanate of general formula **(V)** is not commercially available it can be prepared from the corresponding amine of general formula **(VIII)** in an analogous procedure to that described above for the preparation of **(VI)**. Reaction of these isocyanates with **(IV)** would again yield the requisite ureas of general formula **(I)** wherein $R^1 = R^2 = H$:

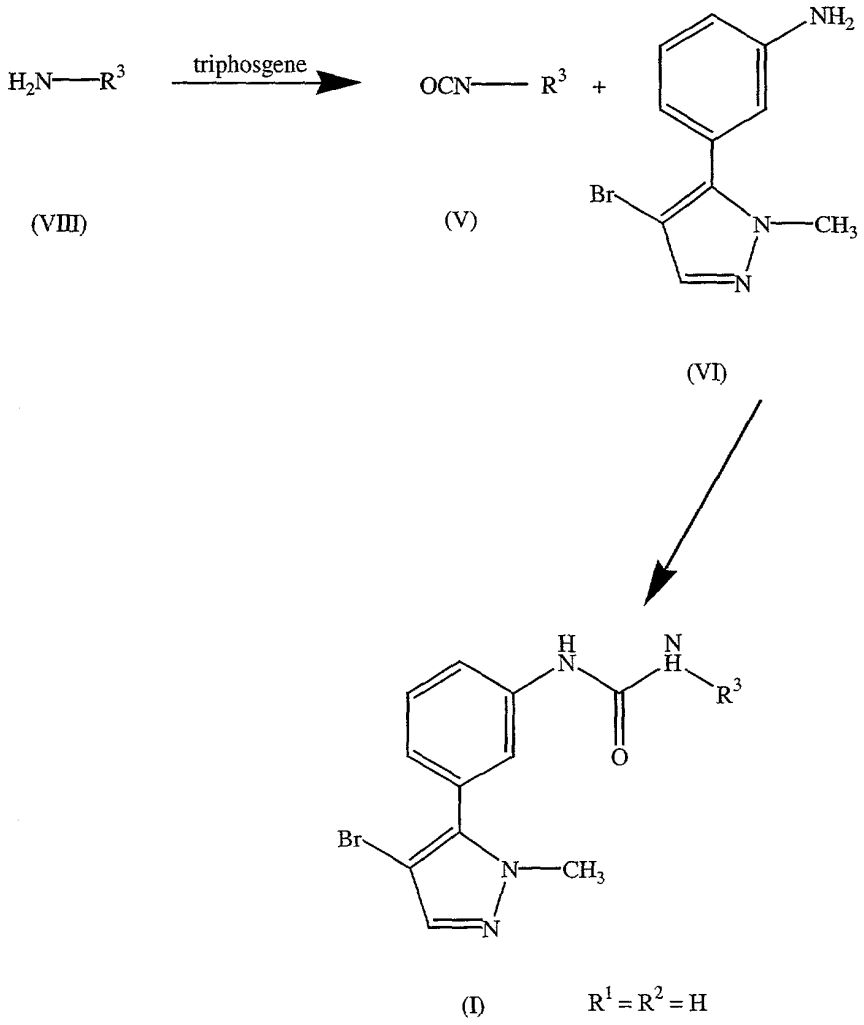
[



(VIII) (V) (VI)



(I) $R^1 = R^2 = H$]

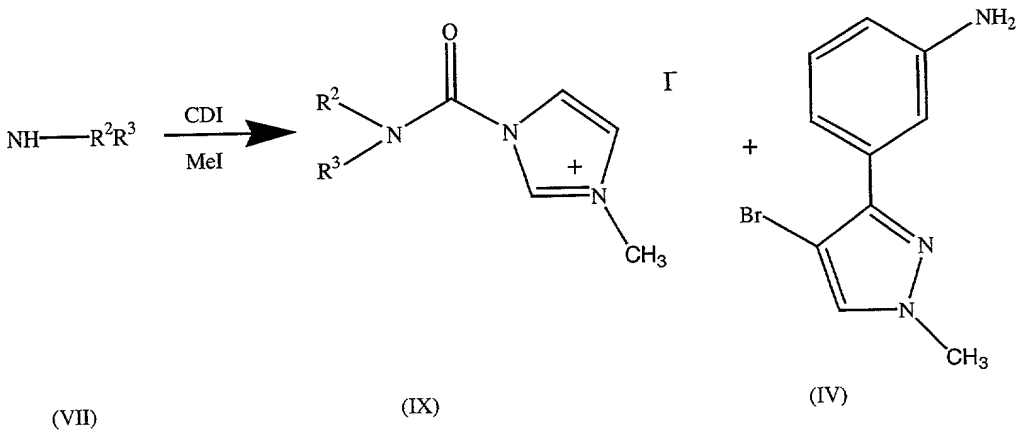


Please amend the paragraph spanning page 57, line 2, to page 58, line 1, as follows:

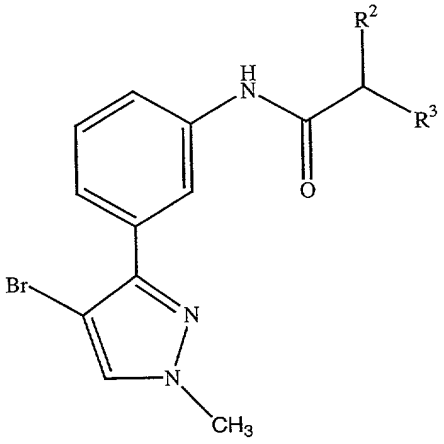
Amines of general formula **(VII)** are also readily converted to activated isocyanate equivalents of general formula **(IX)** by the sequential action of carbonyldiimidazole and methyl iodide in tetrahydrofuran and acetonitrile respectively (R.A. Batey *et al*, *Tetrahedron Lett.*, (1998), 39, 6267-

6270.) Reaction of **(IX)** with **(IV)** in an inert solvent such as a halocarbon would yield the requisite ureas of general formula **(I)** wherein R^1 = H:

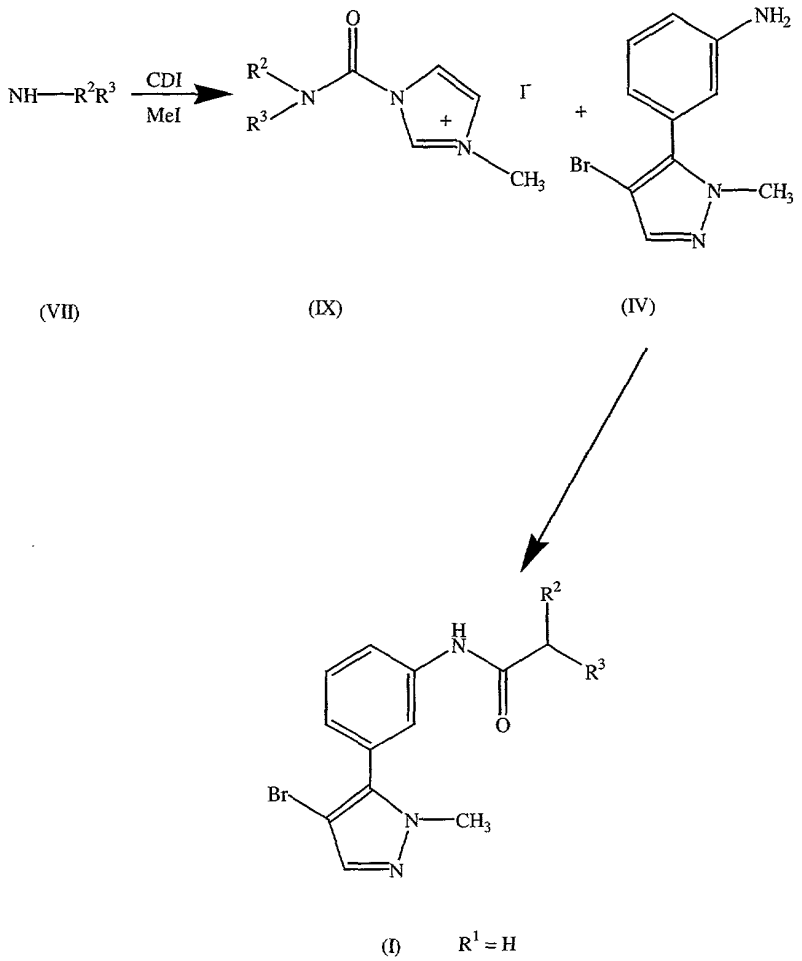
[



(VII) (IX) (IV)



(I) $R^1 = H$]

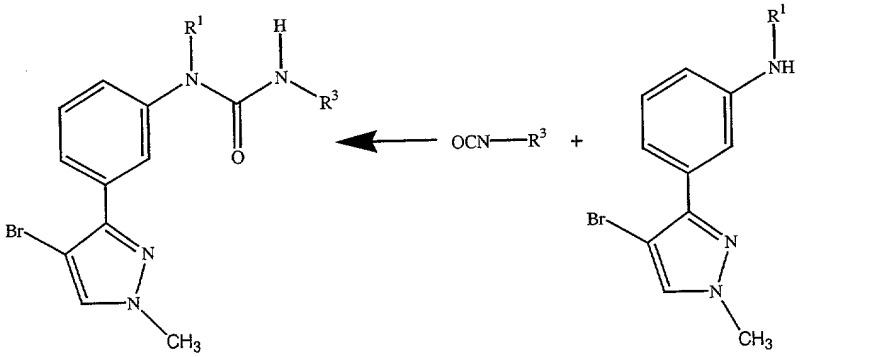


Please amend the paragraph spanning page 58, line 2, to page 59, line 1, as follows:

Amine **(IV)** may be monomethylated according to the procedure of J. Barluenga *et al*, *J. Chem. Soc., Chem. Commun.*, (1984), 20, 1334-1335, or alkylated according to the procedure of P. Marchini *et al*, *J. Org. Chem.*, (1975), 40(23), 3453-3456, to yield compounds of general formula **(X)** wherein R^1 = lower alkyl. These materials may be reacted as above with reagents of general formula **(V)** and **(IX)** as

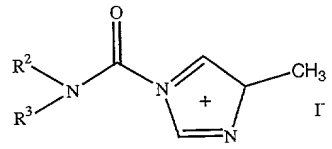
depicted below:

[

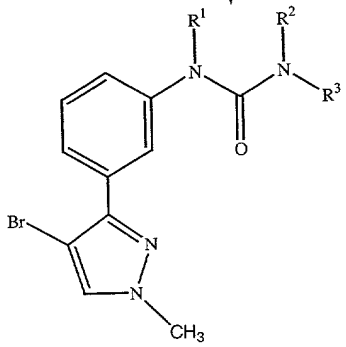


(I) R^1 = lower alkyl, R^2 = H (V) (X) R^1 = lower alkyl

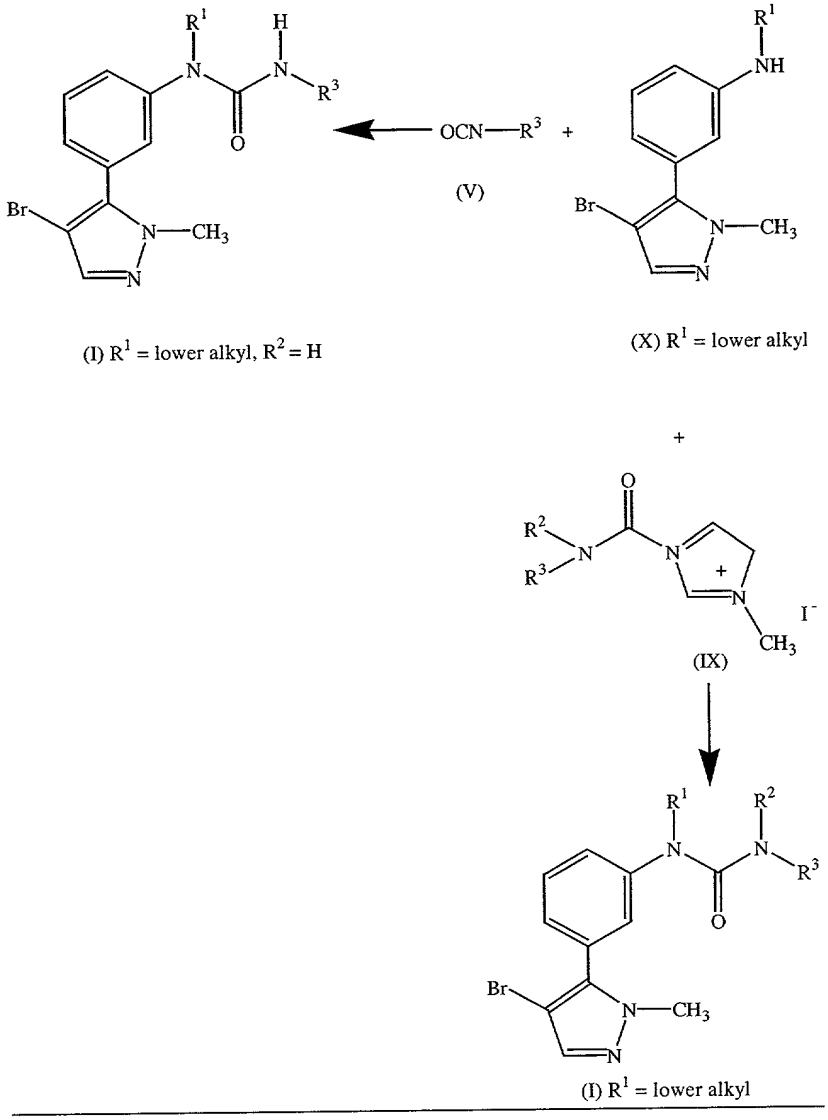
+



(IX)

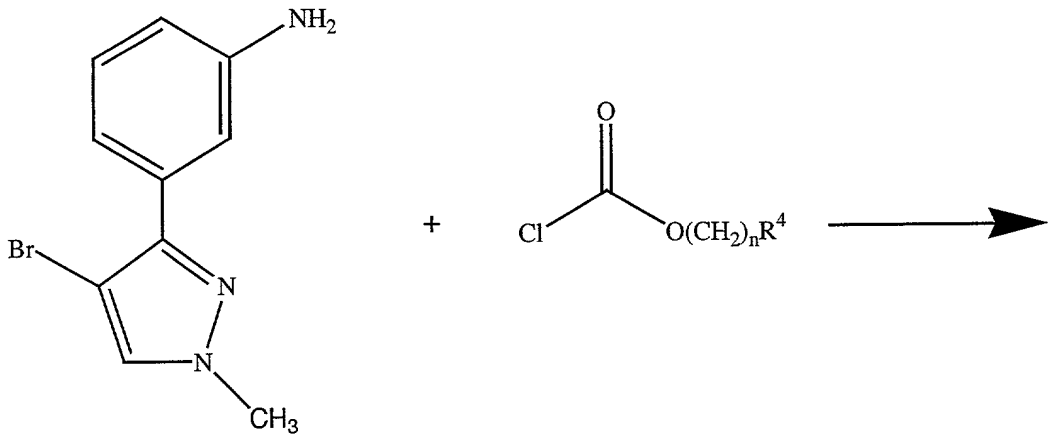


(I) R^1 = lower alkyl]

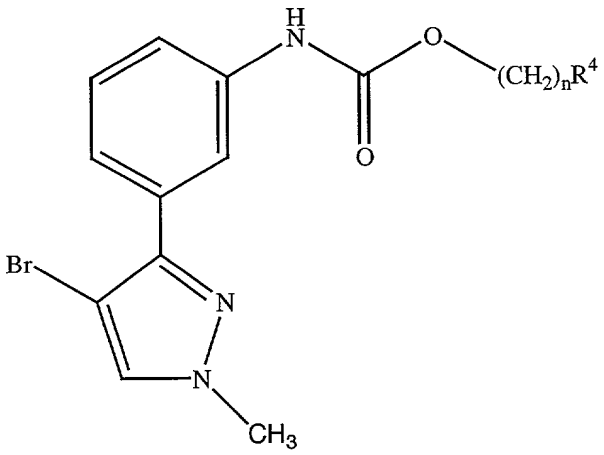


Please amend the paragraph on page 60, line 3, as follows:

[

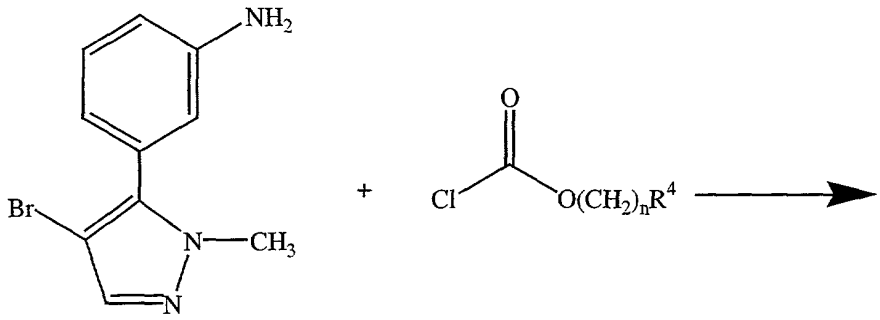


(IV)

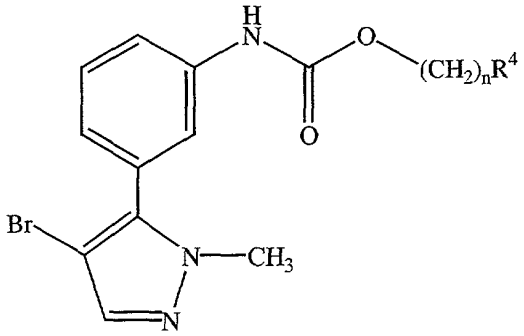


(II) $R^1 = H$

]



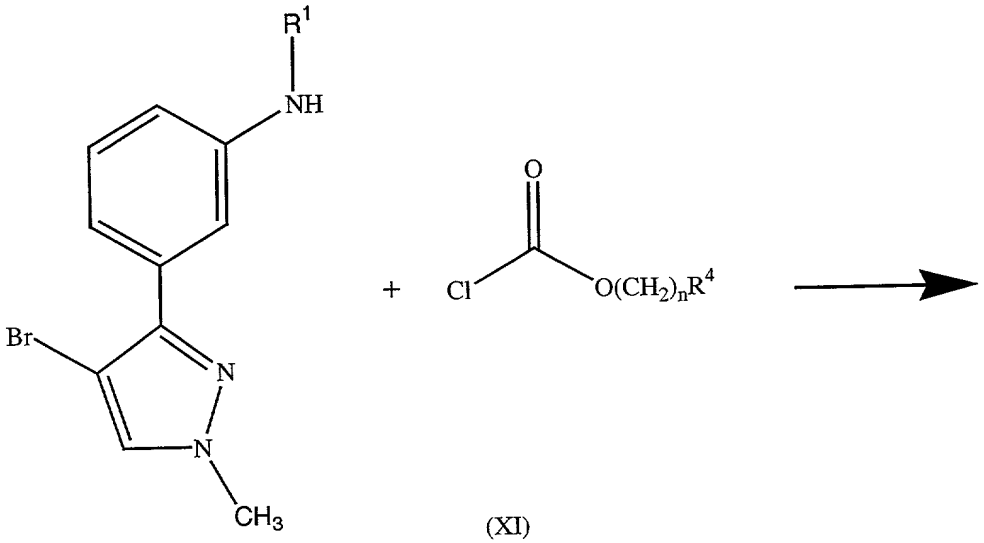
(IV)



(II) $R^1 = H$

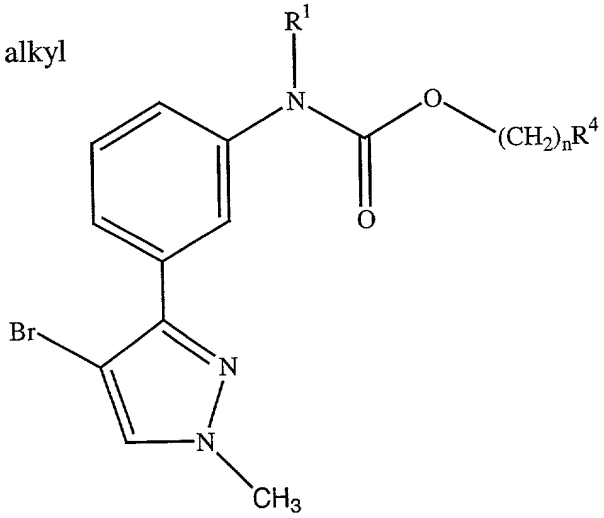
Please amend the paragraph on page 60, line 4, as follows:

[



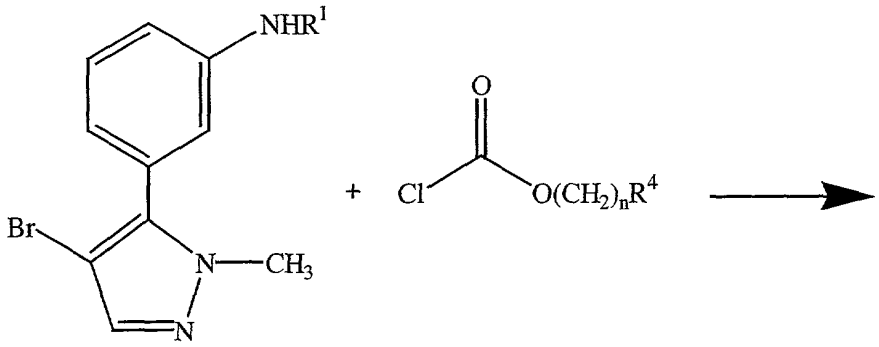
(XI)

(X) R^1 = lower alkyl

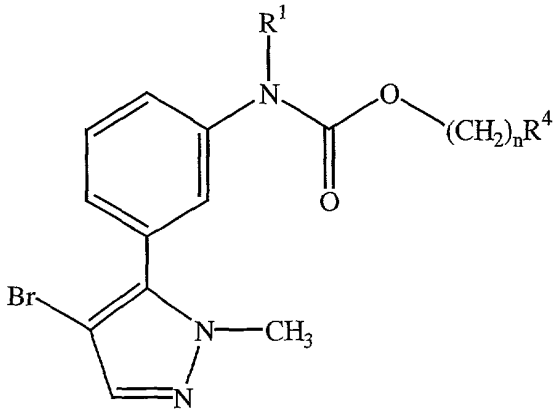


(II) R^1 = lower alkyl

]



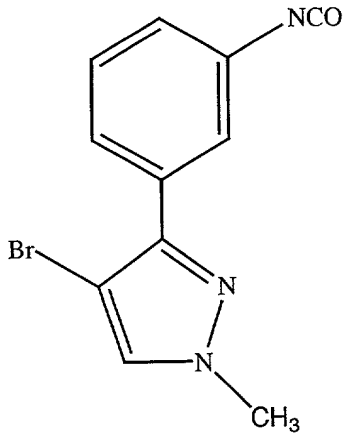
(X) R^1 = lower alkyl (XI)



(II) R^1 = lower alkyl

Please amend the paragraph on page 61, line 1, as follows:

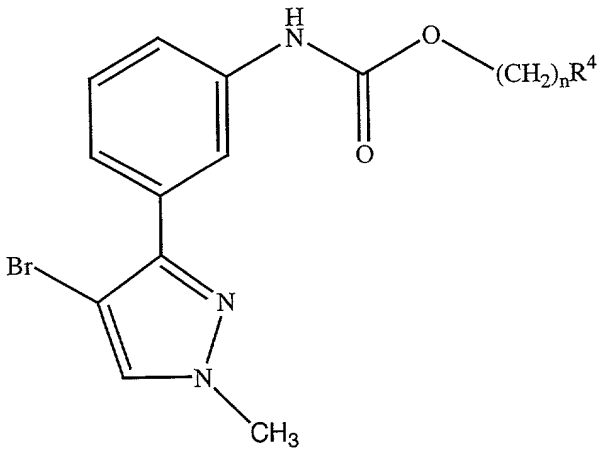
[



(VI)

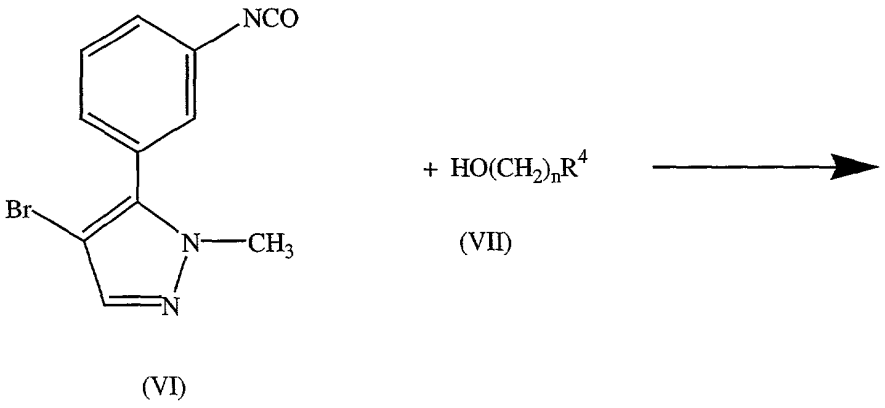
+ $HO(CH_2)_nR^4$ ⟶

(XII)

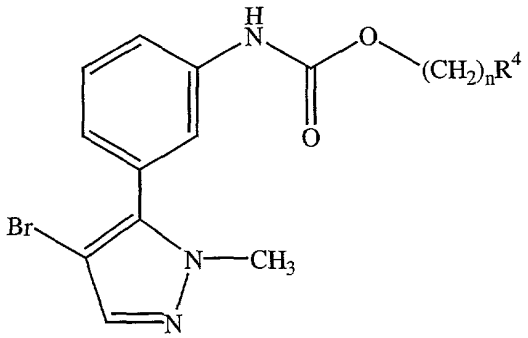


(II) $R^1 = H$

]



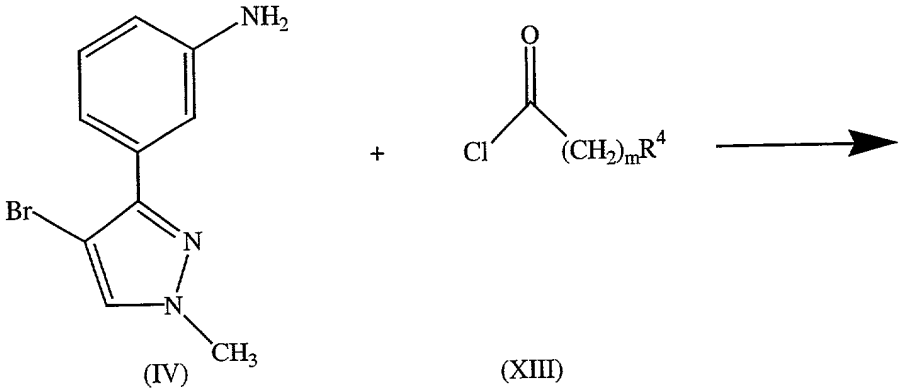
(VI)



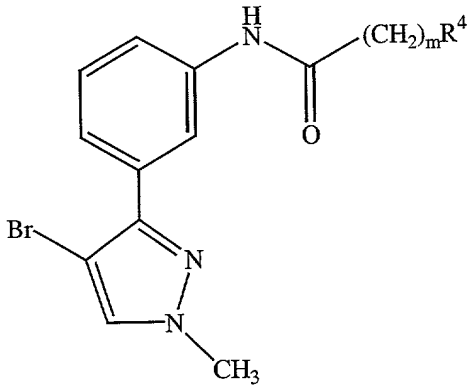
(II) $R^1 = H$

Please amend the paragraph on page 62, line 1, as follows:

[

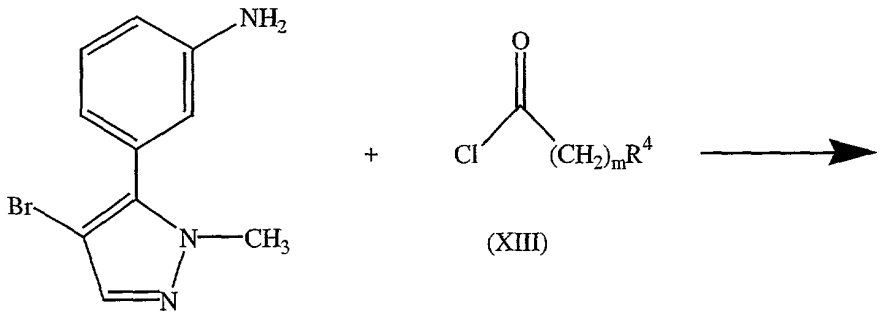


(IV) (XIII)

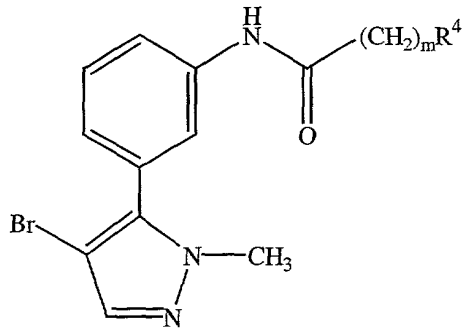


(III) $R^1 = H$

]



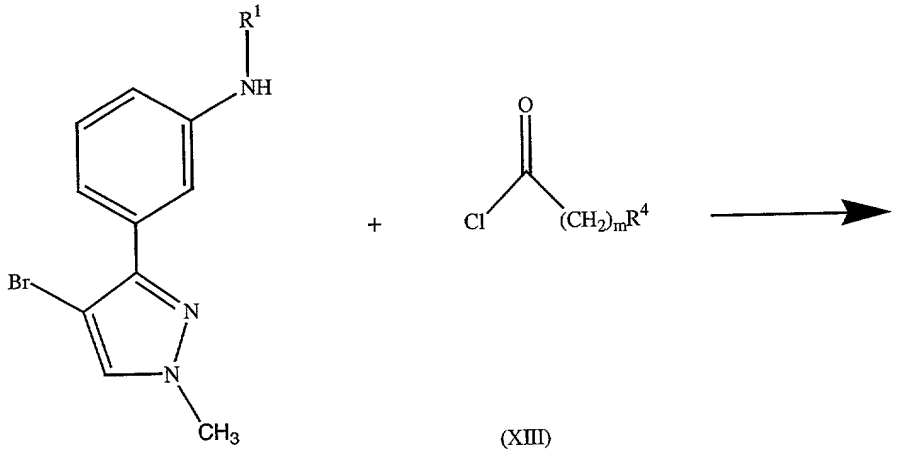
(IV) (XIII)



(III) $R^1 = H$

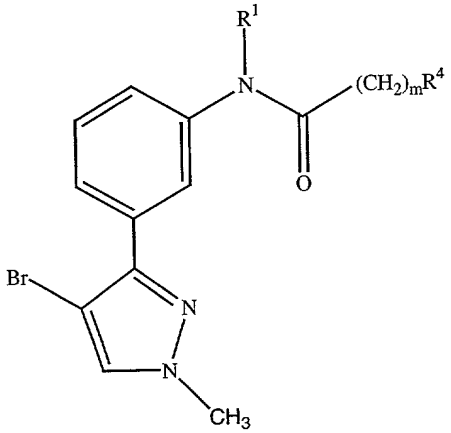
Please amend the paragraph on page 61, line 2, as follows:

[



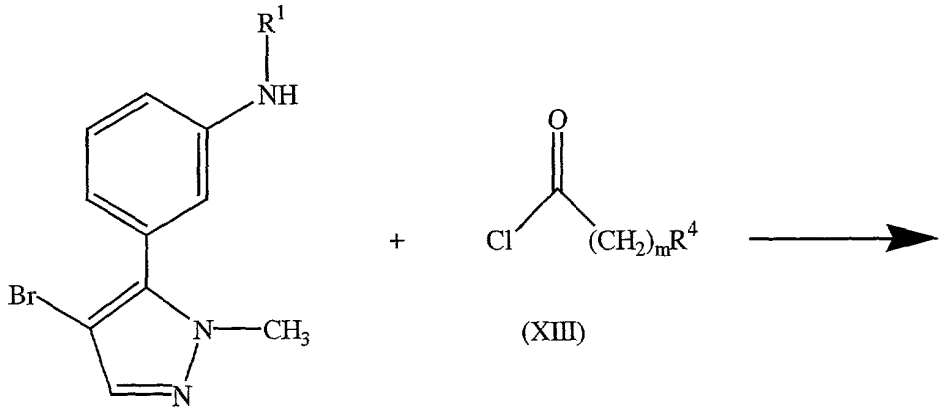
(X) R^1 = lower alkyl

(XIII)



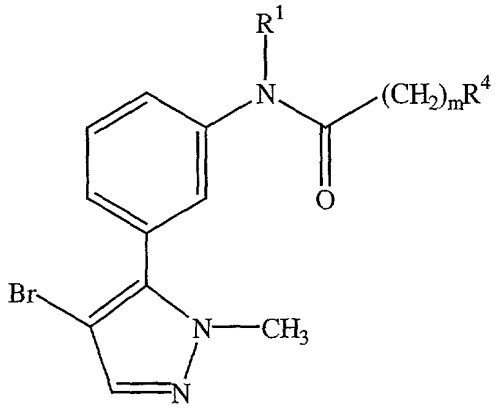
(III) R^1 = lower alkyl

]



(X) R^1 = lower alkyl

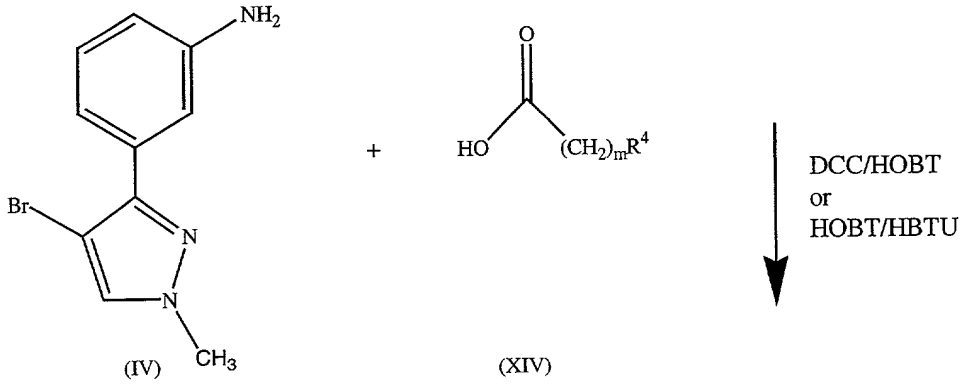
(XIII)

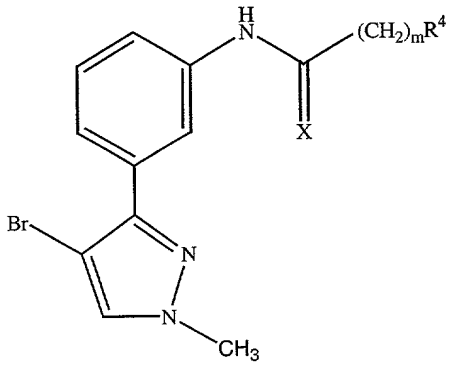


(III) R^1 = lower alkyl

Please amend page 63, line 1 as follows:

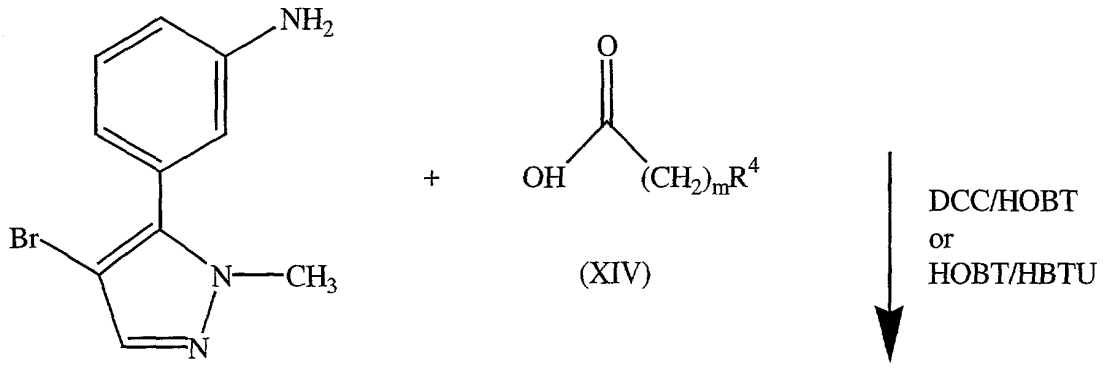
[


NH2
Br
N
N
CH3
(IV)
+
O
HO
(CH2)mR4
(XIV)
DCC/HOBT
or
HOBT/HBTU

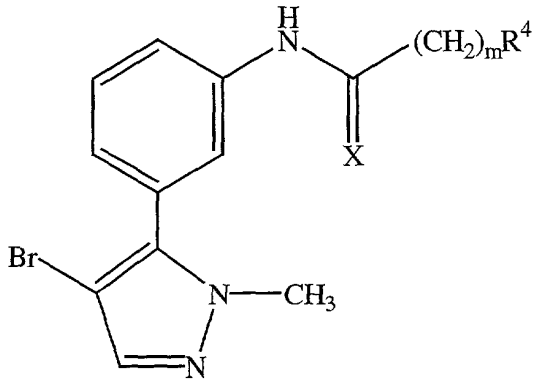

H
N
(CH2)mR4
X
Br
N
N
CH3

(III) $R^1 = H$

]



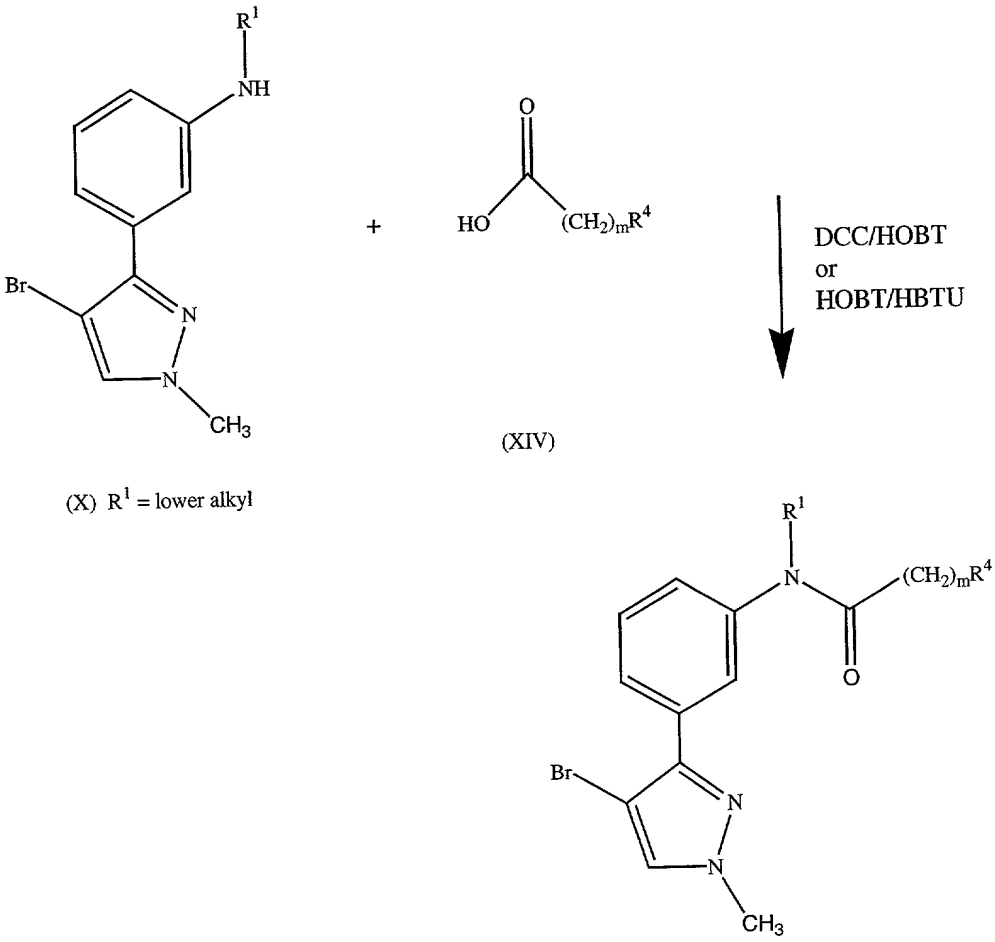
(IV) (XIV)



(III) $R^1 = H$

Please amend page 63, line 5, as follows:

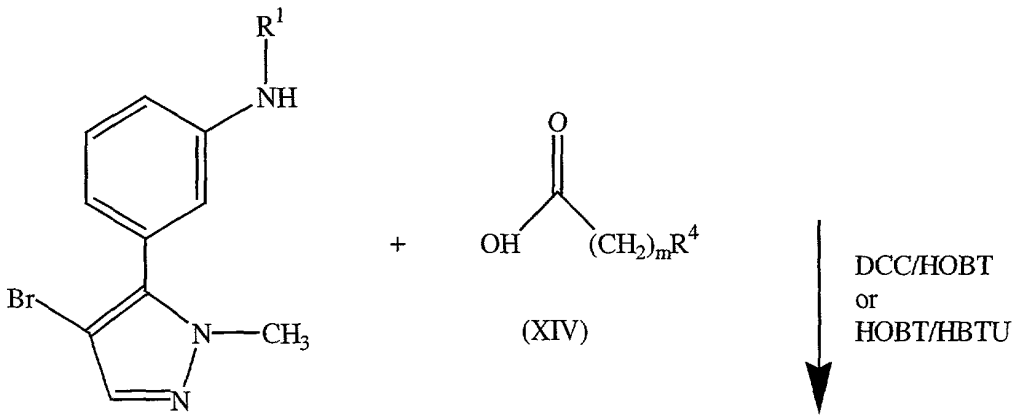
[



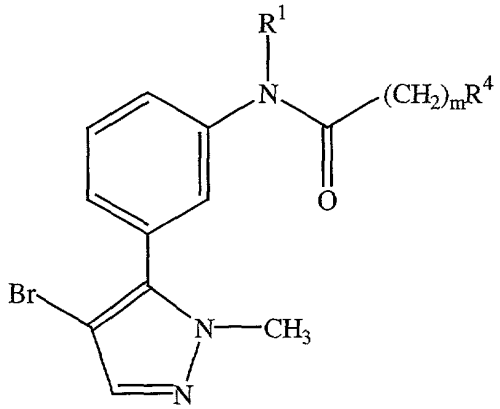
(X) R^1 = lower alkyl

(III) R^1 = lower alkyl

]



(X) R^1 = lower alkyl



(III) R^1 = lower alkyl

Please amend the paragraph on page 66, line 28 to page 67, line 2, as follows:

Experiment 2

Preparation and Analysis of 116100

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][4-methoxyphenoxy]carboxamide

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl][4-methoxyphenoxy]carboxamide]

To 4-methoxyphenylchloroformate (19 mg, 0.10 mmol) in CH_2Cl_2 (0.5 mL) was added dropwise a solution 3-(3-aminophenyl)-4-bromo-2-methylpyrazole [3-(3-aminophenyl)-4-bromo-1-methylpyrazole] (25 mg, 0.10 mmol) and triethylamine (14 μL, 0.10 mmol) in CH_2Cl_2 (0.5 mL). The mixture was stirred for 16 h and concentrated. Chromatography on flash silica (40% EtOAc/hexane) gave the title compound as a colourless solid (21 mg, 52%), m.p. 140.3-141.8°C. (EtOAc/hexane).

Please amend the paragraph on page 67, lines 9-17, as follows:

Experiment 3

Preparation and Analysis of 116101

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][4-trifluoromethoxyphenyl]carboxamide

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl][4-trifluoromethoxyphenyl]carboxamide]

To 4-(trifluoromethoxy)benzoyl chloride (19 μL, 0.12 mmol) in CH_2Cl_2 (1 mL) was added dropwise a solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole [3-(3-aminophenyl)-4-bromo-1-methylpyrazole] (30 mg, 0.12 mmol) and triethylamine (17 μL, 0.12 mmol) in CH_2Cl_2 (0.5 mL). The reaction mixture was stirred for 16 h and concentrated. Chromatography on flash silica (50% EtOAc/hexane) gave the title compound as a colourless solid (40 mg, 76%), m.p. 138.6-139.6 °C (EtOAc/hexane).

Please amend the paragraph on page 67, lines 23-30, as follows:

Experiment 4

Preparation and Analysis of 116102

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][2-thienyl]carboxamide

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl][2-thienyl]carboxamide]

To thiophene-2-carbonyl chloride (11 μL, 0.09 mmol) in CH_2Cl_2 (1 mL) was added dropwise a solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole [3-(3-aminophenyl)-4-bromo-1-methylpyrazole] (25 mg, 0.09 mmol) and triethylamine (14 μL, 0.09 mmol) in CH_2Cl_2 (0.5 mL). The reaction mixture was stirred for 16 h and concentrated. Chromatography on flash silica (50% EtOAc/hexane) gave the title compound as a colourless solid (24 mg, 68%), m.p. 127.8-128.6 °C (EtOAc/hexane).

Please amend the paragraph on page 68, lines 5-14, as follows:

Experiment 5

Preparation and Analysis of 116115

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][{(4-trifluoromethoxy)phenyl)methyl}amino] carboxamide

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl][{(4-trifluoromethoxy)phenyl) methyl}amino]carboxamide]

To a stirred solution of triphosgene (12 mg, 0.04 mmol) in CH_2Cl_2 (0.5 mL) was added dropwise a solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole [3-(3-aminophenyl)-4-bromo-1-methylpyrazole] (30 mg, 0.12 mmol) and triethylamine (33 μL, 0.24 mmol) in CH_2Cl_2 (0.5 mL). After 1 h, 4-(trifluoromethoxy)benzylamine (23 mg, 0.12 mmol) was added. The reaction mixture was stirred for 16 h and concentrated. Chromatography on flash silica (75% EtOAc/hexane) gave the title compound as a colourless solid (38 mg, 68%), m.p. 144.6-145.8 °C (EtOAc/hexane).

Please amend the paragraph on page 68, lines 21-28, as follows:

Experiment 6

Preparation and Analysis of 116120

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][4-chlorophenyl]carboxamide

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl][4-chlorophenyl]carboxamide]

To 4-chlorobenzoyl chloride (15 mg, 0.08 mmol) in CH_2Cl_2 (1 mL) was added dropwise a solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole [3-(3-aminophenyl)-4-bromo-1-methylpyrazole] (21 mg, 0.08 mmol) and triethylamine (12 μL, 0.08 mmol) in CH_2Cl_2 (0.5 mL). The mixture was stirred for 16 h and concentrated. Chromatography on flash silica (50% EtOAc/hexane) gave the title compound as a colourless solid (23 mg, 72%), m.p. 184.4-184.8 °C (EtOAc/hexane).

Please amend the paragraph on page 69, lines 1-33, as follows:

Experiment 7

Preparation and Analysis of 116137

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-[4-(trifluoromethoxy)phenyl]acetamide

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-2-[4-(trifluoromethoxy)phenyl]acetamide]

A solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole [3-(3-aminophenyl)-4-bromo-1-methylpyrazole] (35 mg, 0.14 mmol) and triethylamine (23 μL, 0.17 mmol) in DMF (0.5 mL) was added in one portion to a stirred solution of 4-trifluoromethoxyphenylacetic acid (31 mg, 0.14 mmol), HBTU (53 mg, 0.14 mmol) and HOBT (19 mg, 0.14 mmol) in DMF (1 mL). The mixture was heated at 70 °C for 24 h and then quenched with aqueous sodium bicarbonate solution. Ethyl acetate was added and the organic phase separated, washed with water (.times.3), brine, dried ($MgSO_4$) and evaporated. Chromatography on flash silica (50% EtOAc/hexane) gave the title compound as a colourless solid (43 mg, 68%). m.p. 141.2-142.5 °C (EtOAc/hexane).

Please amend the paragraph on page 69, lines 21-33, as follows:

Experiment 8

Preparation and Analysis of 116174

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(3-fluorophenyl)acetamide

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-2-(3-fluorophenyl)acetamide]

A mixture of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole [3-(3-aminophenyl)-4-bromo-1-methylpyrazole] (30 mg, 0.12 mmol), 3-fluorophenylacetic acid (18 mg, 0.12 mmol), 1-hydroxybenzotriazole hydrate (16 mg, 0.12 mmol) and 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluoro-phosphate (46 mg, 0.12 mmol) were dissolved in chloroform (1.5 ml). N,N-Diisopropylethylamine (0.02 ml, 0.13 mmol) was added and the mixture stirred at room temperature for 16 h. The reaction mixture was then poured into brine and the organic layer washed with further brine, dried over magnesium sulphate and then concentrated in vacuo. The crude product was purified by column chromatography (ethyl acetate-toluene, 1:1), giving the title compound (12 mg, 26%). Rf 0.41 (ethyl acetate-toluene, 1:1).

Please amend the paragraph on page 70, lines 5-16, as follows:

Experiment 9

Preparation and Analysis of 116175

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(3-methoxyphenyl)acetamide

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-2-(3-methoxyphenyl)acetamide]

A solution of 3-methoxyphenylacetyl chloride (0.02 ml, 0.12 mmol) in dichloromethane (0.75 ml) was added dropwise at 0 °C to a solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole [3-(3-aminophenyl)-4-bromo-1-methylpyrazole] (30 mg, 0.12 mmol) and triethylamine (0.02 ml, 0.13 mmol) in dichloromethane (0.75 ml). The resulting mixture was stirred at room temperature for 16 h and then poured into brine. The organic layer was washed with more brine then dried over magnesium sulphate and concentrated in vacuo. The crude product was purified by column chromatography (ethyl acetate-toluene, 1:1), giving the title compound (9 mg, 19%). Rf 0.30 (ethyl acetate-toluene, 1:1).

Please amend the paragraph on page 71, lines 21-33, as follows:

Experiment 10

Preparation and Analysis of 116176

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(2-fluorophenyl)acetamide

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-2-(2-fluorophenyl)acetamide]

A mixture of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole [3-(3-aminophenyl)-4-bromo-1-methylpyrazole] (30 mg, 0.12 mmol), 2-fluorophenylacetic acid (18 mg, 0.12 mmol), 1-hydroxybenzotriazole hydrate (16 mg, 0.12 mmol) and 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluoro-phosphate (46 mg, 0.12 mmol) were dissolved in chloroform (1.5 ml). N,N-Diisopropylethylamine (0.02 ml, 0.13 mmol) was added and the mixture stirred at room temperature for 16 h. The reaction mixture was then poured into brine and the organic layer washed with further brine, dried over magnesium sulphate and then concentrated in vacuo. The crude product was purified by column chromatography (ethyl acetate-toluene, 1:1), giving the title compound (15 mg, 32%). Rf 0.52 (ethyl acetate-toluene, 1:1).

Please amend the paragraph on page 71, lines 5-17, as follows:

Experiment 11

Preparation and Analysis of 116177

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(4-nitrophenyl)acetamide

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-2-(4-nitrophenyl)acetamide]

A mixture of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole [3-(3-aminophenyl)-4-bromo-1-methylpyrazole] (30 mg, 0.12 mmol), 4-nitrophenylacetic acid (22 mg, 0.12 mmol), 1-hydroxybenzotriazole hydrate (16 mg, 0.12 mmol) and 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (46 mg, 0.12 mmol) were dissolved in chloroform (1.5 ml). N,N-Diisopropylethylamine (0.02 ml, 0.13 mmol) was added and the mixture stirred at room temperature for 16 h. The reaction mixture was then poured into brine and the organic layer washed with further brine, dried over magnesium sulphate and then concentrated in vacuo. The crude product was purified by column chromatography (ethyl acetate-toluene, 1:1), giving the title compound (9 mg, 18%). Rf 0.19 (ethyl acetate-toluene, 1:1).

Please amend the paragraph on page 71, line 22, to page 72, line 2, as follows:

Experiment 12

Preparation and Analysis of 116178

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-2-(2-methoxyphenyl)acetamide

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-2-(2-methoxyphenyl)acetamide]

A mixture of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole [3-(3-aminophenyl)-4-bromo-1-methylpyrazole] (30 mg, 0.12 mmol), 2-methoxyphenylacetic acid (20 mg, 0.12 mmol), 1-hydroxybenzotriazole hydrate (16 mg, 0.12 mmol) and 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (46 mg, 0.12 mmol) were dissolved in chloroform (1.5 ml). N,N-Diisopropylethylamine (0.02 ml, 0.13 mmol) was added and the mixture stirred at room temperature for 16 h. The reaction mixture was then poured into brine and the organic layer washed with further brine, dried over magnesium sulphate and then concentrated in vacuo. The crude product was purified by column chromatography (chloroform-methanol, 99:1), giving the title compound (18 mg, 38%) as a colourless solid. Rf 0.65 (chloroform-methanol, 98:2).

Please amend the paragraph on page 72, lines 8-15, as follows:

Experiment 13

Preparation and Analysis of 116192

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(1,1-dimethylethoxy)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(1,1-dimethylethoxy)carboxamide]

To di-tert-butyl dicarbonate (36 mg, 0.17 mmol) in methanol (1 mL) was added dropwise a solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole [3-(3-aminophenyl)-4-bromo-1-methylpyrazole] (42 mg, 0.17 mmol) in methanol (1 mL). The mixture was stirred for 16 h and

concentrated. Chromatography on flash silica (40% EtOAc/hexane) gave the title compound as a colourless solid (29 mg, 49%) (EtOAc/hexane).

Please amend the paragraph on page 72, lines 22 to page 73, line 2, as follows:

One or the other (as indicated) of the two following synthetic protocols was used to generate each of the compounds below:

Protocol A:

To an isocyanate (1 mmol) in CH_2Cl_2 (4 mL) was added dropwise a solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole [3-(3-aminophenyl)-4-bromo-1-methylpyrazole] (1 mmol) in CH_2Cl_2 (4 mL). The mixture was stirred for 16 hours and concentrated. Chromatography on flash silica (20%-80% EtOAc/hexane) followed by recrystallisation gave the pure urea.

Protocol B:

To a stirred solution of triphosgene (0.33 mmol) in CH_2Cl_2 (4 mL) was added dropwise a solution of 3-(3-aminophenyl)-4-bromo-2-methylpyrazole [3-(3-aminophenyl)-4-bromo-1-methylpyrazole] (1 mmol) and triethylamine (2 mmol) in CH_2Cl_2 (4 mL). After 1 hour, an aniline was added (1 mmol). The reaction mixture was stirred for 16 hours and concentrated. Chromatography on flash silica (20%-80% EtOAc/hexane) followed by recrystallisation gave the pure urea.

Please amend the paragraph on page 73, lines 5-8, as follows:

Experiment 14

Preparation and Analysis of 116079

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][(4-methylthiophenyl)amino]carboxamide

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl][(4-methylthiophenyl)amino]carboxamide]

Please amend the paragraph on page 73, lines 16-18, as follows:

Experiment 15

Preparation and Analysis of 116081

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl][(4-chlorophenyl)amino]carboxamide

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl][(4-chlorophenyl)amino]carboxamide]

Please amend the paragraph on page 73, lines 29-31, as follows:

Experiment 16

Preparation and Analysis of 116082

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(4-fluorophenyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(4-fluorophenyl)carboxamide]

Please amend the paragraph on page 74, lines 6-8, as follows:

Experiment 17

Preparation and Analysis of 116087

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-[2-(trifluoromethoxy)phenyl]carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-[2-(trifluoromethoxy)phenyl]carboxamide]

Please amend the paragraph on page 74, lines 17-19, as follows:

Experiment 18

Preparation and Analysis of 116089

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(2-nitrophenyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(2-nitrophenyl)carboxamide]

Please amend the paragraph on page 74, lines 29-31, as follows:

Experiment 19

Preparation and Analysis of 116091

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(4-methoxyphenyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(4-methoxyphenyl)carboxamide]

Please amend the paragraph on page 75, lines 7-9, as follows:

Experiment 20

Preparation and Analysis of 116092

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(2-methylphenyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(2-methylphenyl)carboxamide]

Please amend the paragraph on page 75, lines 18-20, as follows:

Experiment 21

Preparation and Analysis of 116097

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-[4-(trifluoromethyl)phenyl]carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-[4-(trifluoromethyl)phenyl]carboxamide]

Please amend the paragraph on page 75, lines 28-30, as follows:

Experiment 22

Preparation and Analysis of 116105

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(3-chlorophenyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(3-chlorophenyl)carboxamide]

Please amend the paragraph on page 76, lines 8-10, as follows:

Experiment 23

Preparation and Analysis of 116108

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(2-chlorophenyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(2-chlorophenyl)carboxamide]

Please amend the paragraph on page 76, lines 20-22, as follows:

Experiment 24

Preparation and Analysis of 116110

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-[4-(methylethyl)phenyl]carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-[4-(methylethyl)phenyl]carboxamide]

Please amend the paragraph on page 76, lines 31-33, as follows:

Experiment 25

Preparation and Analysis of 116111

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(3-methoxyphenyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(3-methoxyphenyl)carboxamide]

Please amend the paragraph on page 77, lines 8-10, as follows:

Experiment 26

Preparation and Analysis of 116112

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(3-methylphenyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(3-methylphenyl)carboxamide]

Please amend the paragraph on page 77, lines 19-22, as follows:

Experiment 27

Preparation and Analysis of 116113

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-methyl-N-[4-(trifluoromethoxy)phenyl]-carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-methyl-N-[4-(trifluoromethoxy)phenyl]-carboxamide]

Please amend the paragraph on page 77, lines 30-32, as follows:

Experiment 28

Preparation and Analysis of 116119

N-[4-(tert-butyl)phenyl]{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}carboxamide

[N-[4-(tert-butyl)phenyl]{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}carboxamide]

Please amend the paragraph on page 78, lines 8-10, as follows:

Experiment 29

Preparation and Analysis of 116122

N-[4-(dimethylamino)phenyl]{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}carboxamide

[N-[4-(dimethylamino)phenyl]{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}carboxamide]

Please amend the paragraph on page 78, lines 19-21, as follows:

Experiment 30

Preparation and Analysis of 116138

N-(3,5-dichloro-4-methylphenyl){[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}carboxamide

[N-[4-(dimethylamino)phenyl]{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}carboxamide]

Please amend the paragraph on page 78, lines 30-32, as follows:

Experiment 31

Preparation and Analysis of 116139

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-[4-(trifluoromethylthio)phenyl]carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-[4-(trifluoromethylthio)phenyl]carboxamide]

Please amend the paragraph on page 79, lines 8-10, as follows:

Experiment 32

Preparation and Analysis of 116141

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(cyclohexyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(cyclohexyl)carboxamide]

Please amend the paragraph on page 79, lines 21-23, as follows:

Experiment 33

Preparation and Analysis of 116143

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(phenylmethyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(phenylmethyl)carboxamide]

Please amend the paragraph on page 80, lines 1-3, as follows:

Experiment 34

Preparation and Analysis of 116144

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(2-fluorophenyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(2-fluorophenyl)carboxamide]

Please amend the paragraph on page 80, lines 11-13, as follows:

Experiment 35

Preparation and Analysis of 116145

2-({[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-amino}carbonylamino)benzamide

[2-({[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-amino}carbonylamino)benzamide]

Please amend the paragraph on page 80, lines 21-23, as follows:

Experiment 36

Preparation and Analysis of 116147

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(4-cyanophenyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(4-cyanophenyl)carboxamide]

Please amend the paragraph on page 80, lines 31-33, as follows:

Experiment 37

Preparation and Analysis of 116148

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(2-cyanophenyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(2-cyanophenyl)carboxamide]

Please amend the paragraph on page 81, lines 9-11. as follows:

Experiment 38

Preparation and Analysis of 116182

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(4-fluorophenylmethyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(4-fluorophenylmethyl)carboxamide]

Please amend the paragraph on page 81, lines 21-23, as follows:

Experiment 39

Preparation and Analysis of 116183

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(3,4-dimethoxyphenylmethyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(3,4-dimethoxyphenylmethyl)carboxamide]

Please amend the paragraph on page 82, lines 1-3, as follows:

Experiment 40

Preparation and Analysis of 116184

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(3,4,5-trimethoxyphenylmethyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(3,4,5-trimethoxyphenylmethyl)carboxamide]

Please amend the paragraph on page 82, lines 13-15, as follows:

Experiment 41

Preparation and Analysis of 116185

N-[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]-[{(2-methylphenyl)methyl}amino]carboxamide

[N-[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]-[{(2-methylphenyl)methyl}amino]carboxamide]

Please amend the paragraph on page 826, lines 25-27, as follows:

Experiment 42

Preparation and Analysis of 116189

{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-(4-methoxyphenylmethyl)carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-(4-methoxyphenylmethyl)carboxamide]

Please amend the paragraph on page 83, lines 6-8, as follows:

Experiment 43

Preparation and Analysis of 116194

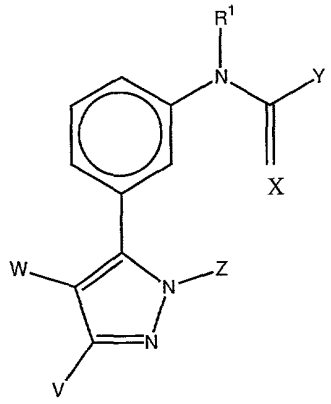
{[3-(4-bromo-2-methylpyrazol-3-yl)phenyl]amino}-N-[2-(4-methoxy)phenylethyl]carboxamide

[{[3-(4-bromo-1-methylpyrazol-3-yl)phenyl]amino}-N-[2-(4-methoxy)phenylethyl]carboxamide]

In the Claims:

Please delete claim 1. Please add new claims 14-26.

14. **(New)** A method for modulating by inverse agonism the activity of a human $5HT_{2A}$ serotonin receptor by contacting the receptor with a compound of formula:



Wherein:

W is lower alkyl (C_{1-6}), or halogen;

V is lower alkyl (C_{1-6}), or halogen;

X is either Oxygen or Sulfur;

Y is NR^2R^3, or $(CH_2)_mR^4$, or $O(CH_2)_nR^4$;

Z is lower alkyl (C_{1-6});

m=0-4

n=0-4

R^1 is H or lower alkyl(C_{1-4});

R^2 is H or lower alkyl(C_{1-4});

R^3 and R^4 are independently a C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, OCF_3, SMe, $COOR^7$, $SO_2NR^5R^6$, SO_3R^7, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, and aryloxy wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, or aryloxy groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, SO_3R^7, $SO_2NR^5R^6$, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl;

R^5 and R^6 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH_2 aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^7R^8$, NR^7R^8, $NHCOCH_3$, OCF_3, SMe, $COOR^9$, SO_3R^7, $SO_2NR^7R^8$, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, or aryl groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^8R^9$, N R^8R^9, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl,

or R^5 and R^6 may form part of a 5, 6 or 7 membered cyclic structure which may be either

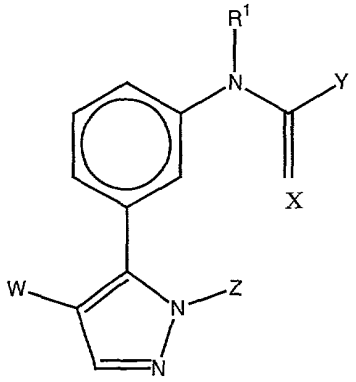
saturated or unsaturated and that may contain up to four heteroatoms selected from O, N or S and said cyclic structure may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, Me, NO_2, OH, OMe, OEt, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, $HCOCH_3$, COEt, COMe, or halogen;

R^7 may be independently selected from H or C_{1-6} alkyl;

R^8 and R^9 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH_2 aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from halogen, CF_3, OCF_3, OEt, CCl_3, Me, NO_2, OH, OMe, SMe, COMe, CN , $COOR^7$, SO_3R^7, COEt, $NHCOCH_3$, or aryl;

an aryl moiety can be a 5 or 6 membered aromatic hetero-cyclic ring (containing up to 4 hetero atoms independently selected from N, O, or S) or a 6 membered aromatic non-heterocyclic ring or a polycycle.

15. **(New)** A method for modulating by inverse agonism the activity of a human $5HT_{2A}$ serotonin receptor by contacting the receptor with a compound of formula:



(B)

Wherein:

W is Me, or Et, or halogen;

X is either Oxygen or Sulfur;

Y is NR^2R^3, or $(CH_2)_mR^4$, or $O(CH_2)_nR^4$;

Z is lower alkyl (C_{1-6});

m=0-4

n=0-4

R^1 is H or lower alkyl (C_{1-4});

R^2 is H or lower alkyl(C_{1-4});

R^3 and R^4 are independently a C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, OCF_3, SMe, $COOR^7$, $SO_2NR^5R^6$, SO_3R^7, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, and aryloxy wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, or aryloxy groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, SO_3R^7, $SO_2NR^5R^6$, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl;

R^5 and R^6 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH, aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^7R^8$, NR^7R^8, $NHCOCH_3$, OCF_3, SMe, $COOR^9$, SO_3R^7, $SO_2NR^7R^8$, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, or aryl groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3 CCl_3, NO_2, OH, $CONR^8R^9$, NR^8R^9, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl,

or R^5 and R^6 may form part of a 5, 6 or 7 membered cyclic structure which may be either saturated or unsaturated and that may contain up to four heteroatoms selected from 0, N or S and

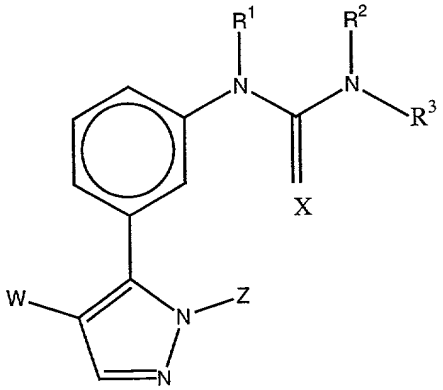
said cyclic structure may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, Me, NO_2, OH, OMe, OEt, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, $NHCOCH_3$, COEt, COMe, or halogen;

R^7 may be independently selected from H or C_{1-6} alkyl;

R^8 and R^9 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH_2aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from halogen, CF_3, OCF_3, OEt, CCl_3, Me, NO_2, OH, OMe, SMe, COMe, CN , $COOR^7$, SO_3R^7, COEt, $NHCOCH_3$, or aryl;

an aryl moiety can be a 5 or 6 membered aromatic hetero-cyclic ring (containing up to 4 hetero atoms independently selected from N, O, or S) or a 6 membered aromatic non-heterocyclic ring or a polycycle.

16. **(New)** A method for modulating by inverse agonism the activity of a human $5HT_{2A}$ serotonin receptor by contacting the receptor with a compound of formula:



(I)

Wherein:

R1 and R2 are H;

W is Br;

X is O;

Z is Me;

R^3 is C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, OCF_3, SMe, $COOR^7$, $SO_2NR^5R^6$, SO_3R^7, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, and aryloxy wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, or aryloxy groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, SO_3R^7, $SO_2NR^5R^6$, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl;

R^5 and R^6 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH, aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^7R^8$, NR^7R^8, $NHCOCH_3$, OCF_3, SMe, $COOR^9$, SO_3R^7, $SO_2NR^7R^8$, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, or aryl groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3 CCl_3, NO_2, OH, $CONR^8R^9$, NR^8R^9, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl,

or R^5 and R^6 may form part of a 5, 6 or 7 membered cyclic structure which may be either saturated or unsaturated and that may contain up to four heteroatoms selected from 0, N or S and said cyclic structure may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, Me, NO_2, OH, OMe, OEt, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, $NHCOCH_3$, COEt, COMe, or halogen;

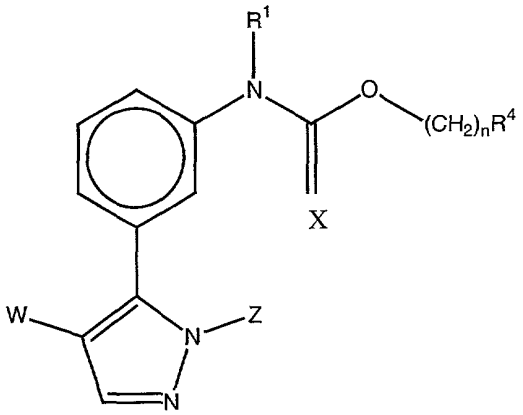
R^7 may be independently selected from H or C_{1-6} alkyl;

R^8 and R^9 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH_2aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from halogen, CF_3, OCF_3, OEt, CCl_3,

Me, NO_2, OH, OMe, SMe, COMe, CN , $COOR^7$, SO_3R^7, COEt, $NHCOCH_3$, or aryl;

an aryl moiety can be a 5 or 6 membered aromatic hetero-cyclic ring (containing up to 4 hetero atoms independently selected from N, O, or S) or a 6 membered aromatic non-heterocyclic ring or a polycycle.

17. **(New)** A method for modulating by inverse agonism the activity of a human $5HT_{2A}$ serotonin receptor by contacting the receptor with a compound of formula:



(II)

Wherein:

W is Br;

X is O;

Z is Me;

R1 is H

M= 0 – 4;

R^4 is C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, OCF_3, SMe, $COOR^7$, $SO_2NR^5R^6$, SO_3R^7, CO-lower alkyl,

SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, and aryloxy wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, or aryloxy groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, SO_3R^7, $SO_2NR^5R^6$, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl;

R^5 and R^6 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH, aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^7R^8$, NR^7R^8, $NHCOCH_3$, OCF_3, SMe, $COOR^9$, SO_3R^7, $SO_2NR^7R^8$, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, or aryl groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3 CCl_3, NO_2, OH, $CONR^8R^9$, NR^8R^9, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl,

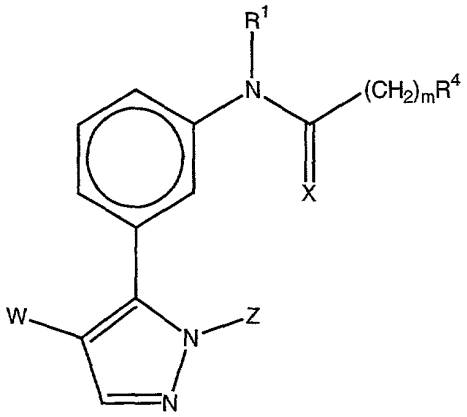
or R^5 and R^6 may form part of a 5, 6 or 7 membered cyclic structure which may be either saturated or unsaturated and that may contain up to four heteroatoms selected from 0, N or S and said cyclic structure may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, Me, NO_2, OH, OMe, OEt, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, $NHCOCH_3$, COEt, COMe, or halogen;

R^7 may be independently selected from H or C_{1-6} alkyl;

R^8 and R^9 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH_2aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from halogen, CF_3, OCF_3, OEt, CCl_3, Me, NO_2, OH, OMe, SMe, COMe, CN , $COOR^7$, SO_3R^7, COEt, $NHCOCH_3$, or aryl;

an aryl moiety can be a 5 or 6 membered aromatic hetero-cyclic ring (containing up to 4 hetero atoms independently selected from N, O, or S) or a 6 membered aromatic non-heterocyclic ring or a polycycle.

18. **(New)** A method for modulating by inverse agonism the activity of a human $5HT_{2A}$ serotonin receptor by contacting the receptor with a compound of formula:



wherein:

W is Br;

X is O;

Z is Me;

R1 is H;

m= 0-4;

R^4 is C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, OCF_3, SMe, $COOR^7$, $SO_2NR^5R^6$, SO_3R^7, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, and aryloxy wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, or aryloxy groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, SO_3R^7, $SO_2NR^5R^6$, CO-lower alkyl, SCF_3CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl;

R^5 and R^6 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or

CH, aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^7R^8$, NR^7R^8, $NHCOCH_3$, OCF_3, SMe, $COOR^9$, SO_3R^7, $SO_2NR^7R^8$, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, or aryl groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3 CCl_3, NO_2, OH, $CONR^8R^9$, NR^8R^9, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl,

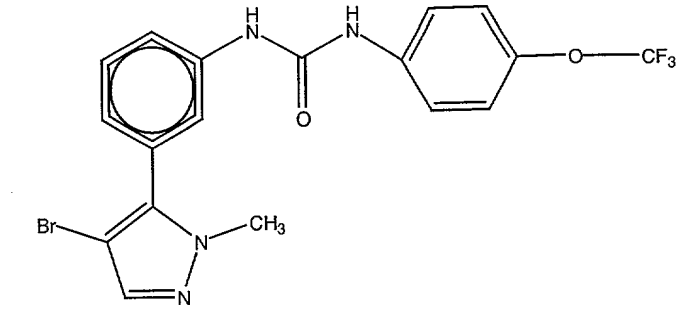
or R^5 and R^6 may form part of a 5, 6 or 7 membered cyclic structure which may be either saturated or unsaturated and that may contain up to four heteroatoms selected from 0, N or S and said cyclic structure may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, Me, NO_2, OH, OMe, OEt, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, $NHCOCH_3$, COEt, COMe, or halogen;

R^7 may be independently selected from H or C_{1-6} alkyl;

R^8 and R^9 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH_2aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from halogen, CF_3, OCF_3, OEt, CCl_3, Me, NO_2, OH, OMe, SMe, COMe, CN , $COOR^7$, SO_3R^7, COEt, $NHCOCH_3$, or aryl;

an aryl moiety can be a 5 or 6 membered aromatic hetero-cyclic ring (containing up to 4 hetero atoms independently selected from N, O, or S) or a 6 membered aromatic non-heterocyclic ring or a polycycle.

19. **(New)** The method of any one of claims 14-18 wherein the compound is selected from the group consisting of:



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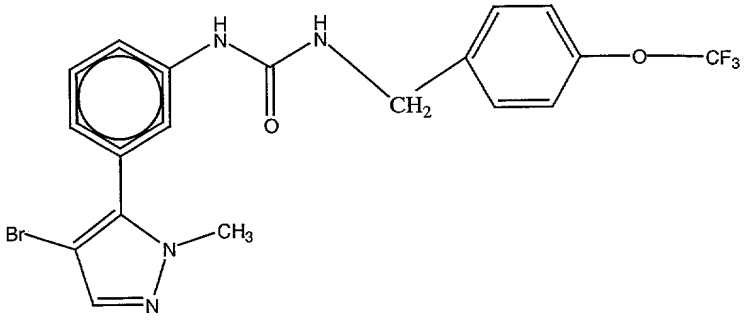

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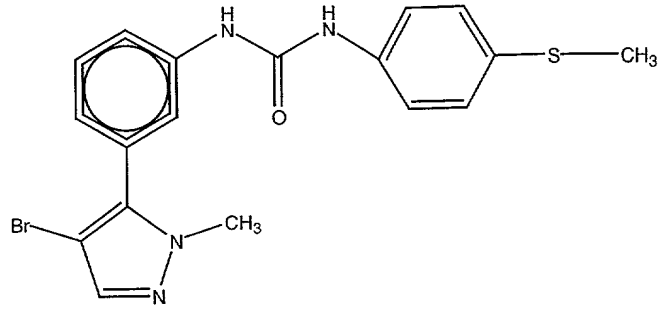

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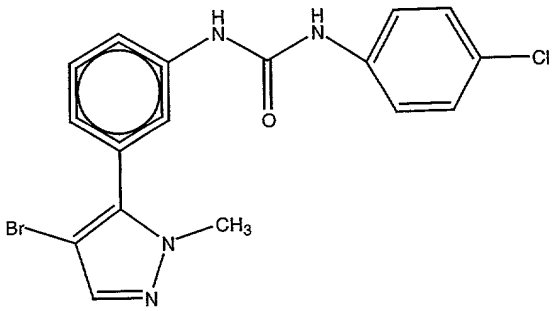

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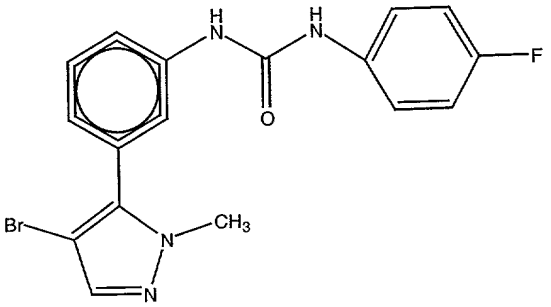

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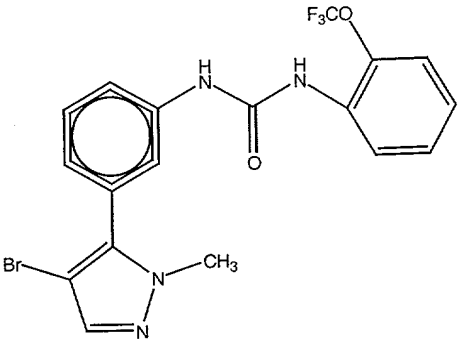

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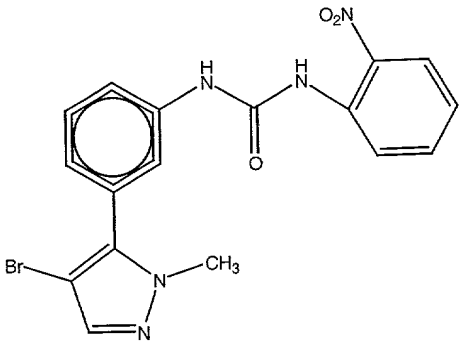

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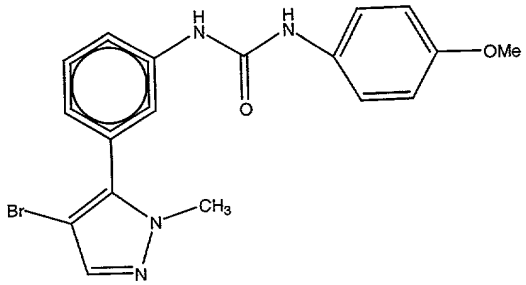
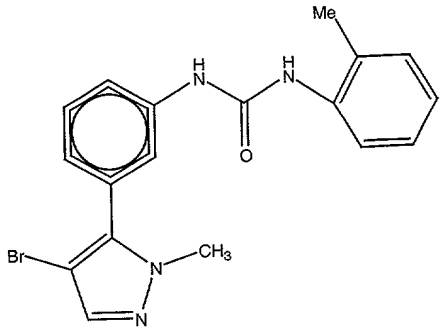

H
N
H
N
OMe
O
Br
N
CH3
N

,


Me
H
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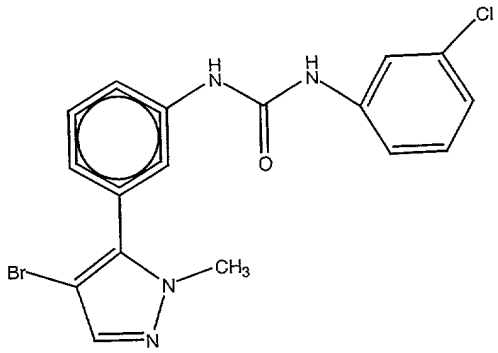
H
N
O
Br
N
CH3
N

,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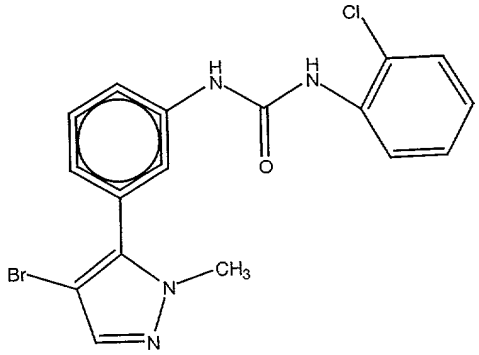
Cl
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O
Br
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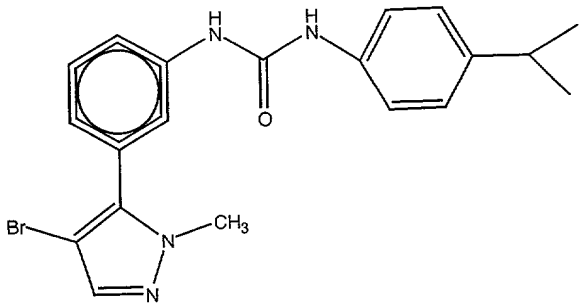
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O
Br
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CH3
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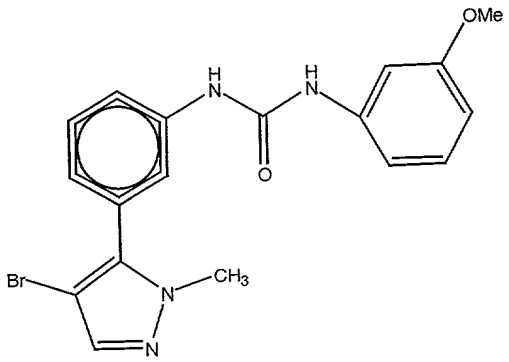
OMe
H
N
H
N
O
Br
N
CH3
N

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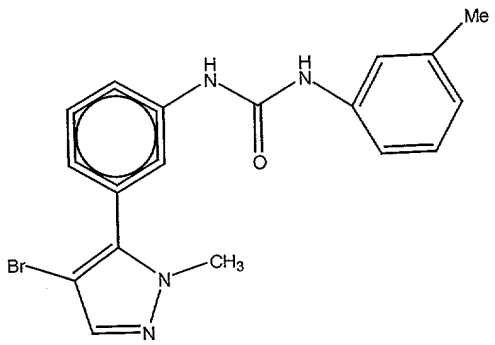
Me
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H
N
O
Br
N
CH3
N

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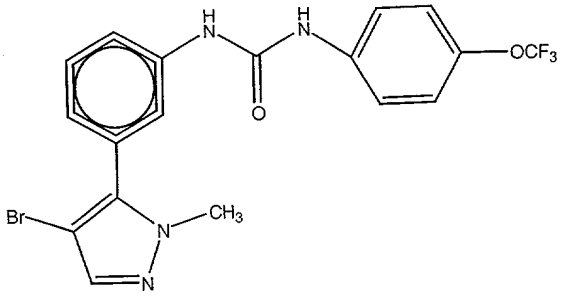
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H
N
O
Br
N
CH3
N

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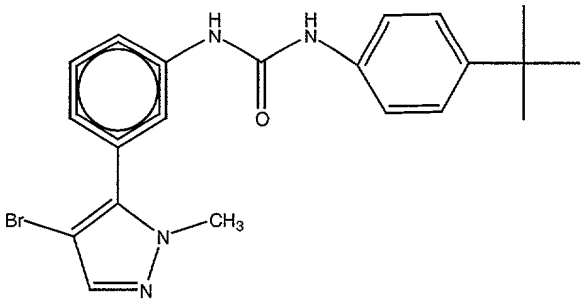

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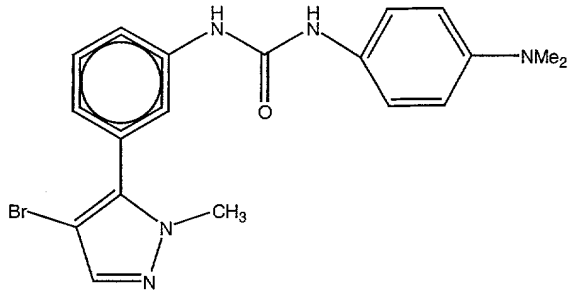

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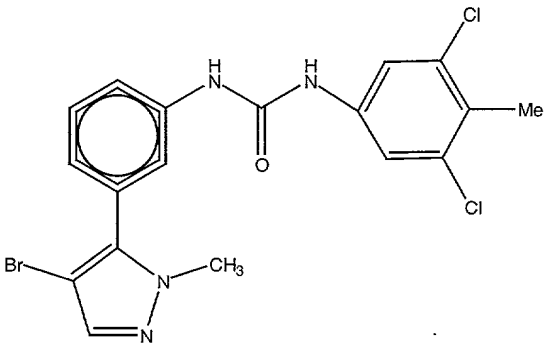

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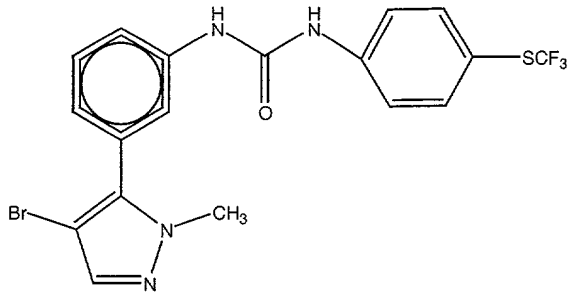

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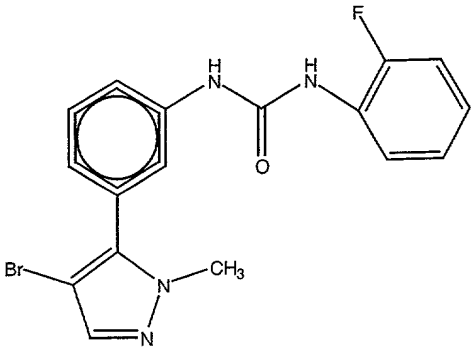
F
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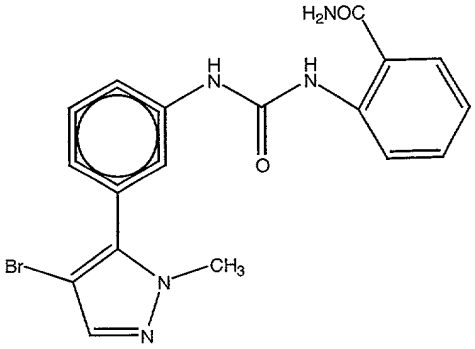
H
N
O
Br
N
CH3
N

,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H
N
O
Br
N
CH3
N

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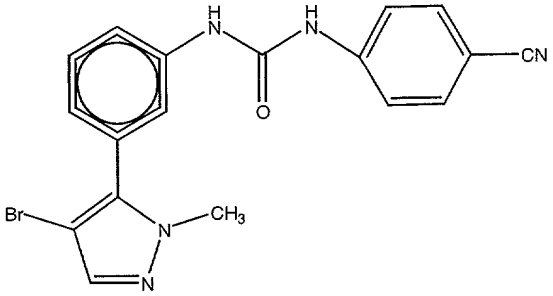
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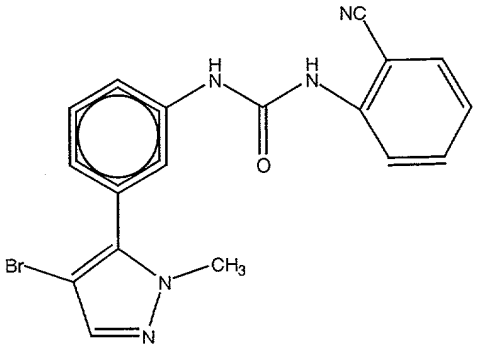
H
N
CN
O
Br
N
CH3
N

,


NC
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H
N
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Br
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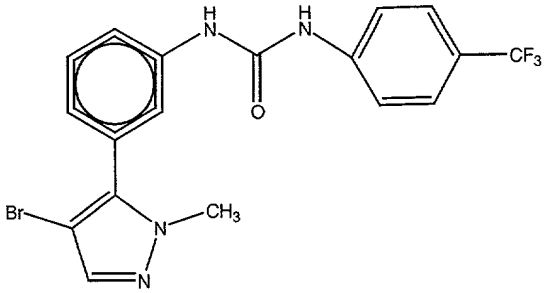
CH3
N

,



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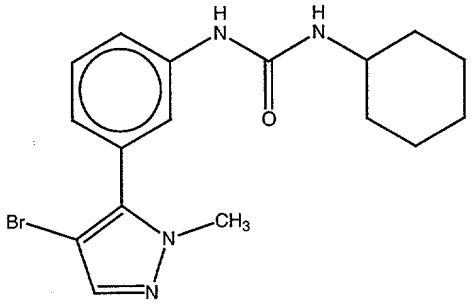

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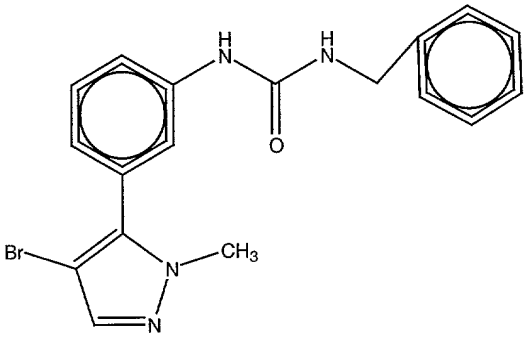

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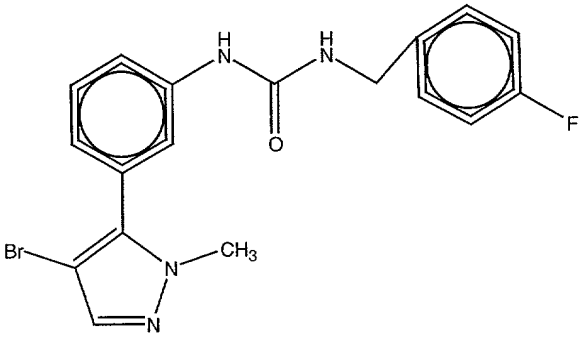

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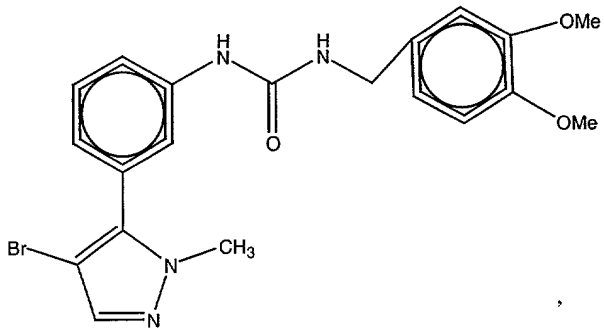
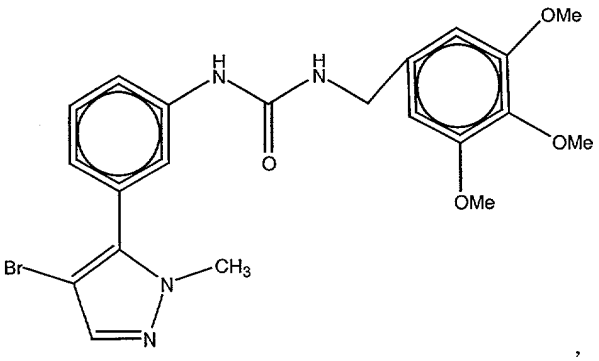
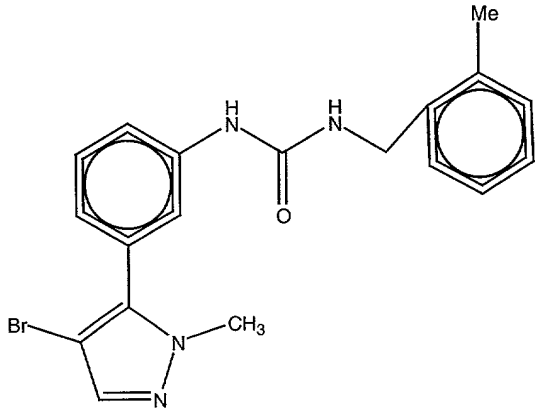

H
N
H
N
O
OMe
OMe
Br
N
CH3
N

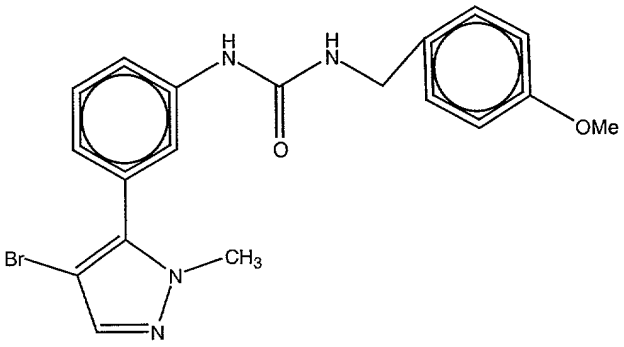
,


H
N
H
N
O
OMe
OMe
OMe
Br
N
CH3
N

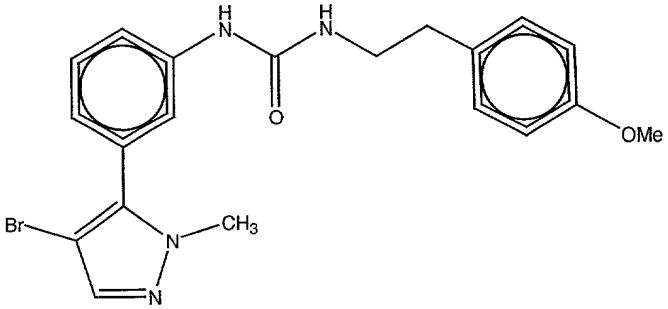
,


Me
H
N
H
N
O
Br
N
CH3
N

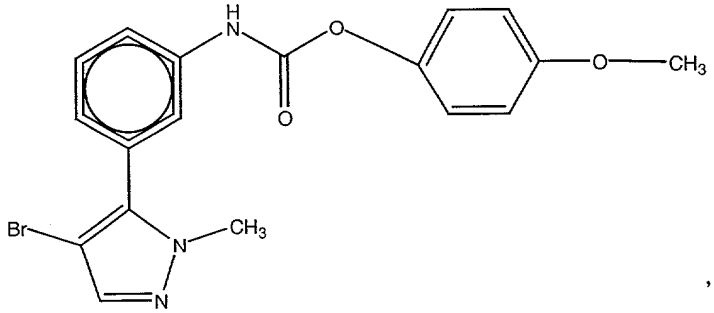
,


H
N
H
N
O
OMe
Br
N
CH3
N

,


H
N
H
N
O
OMe
Br
N
CH3
N

,


H
N
O
O
O
CH3
Br
N
CH3
N

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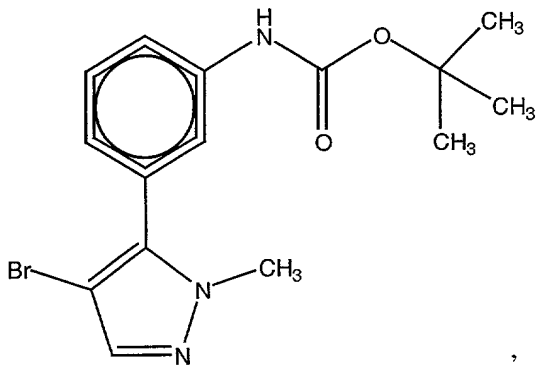

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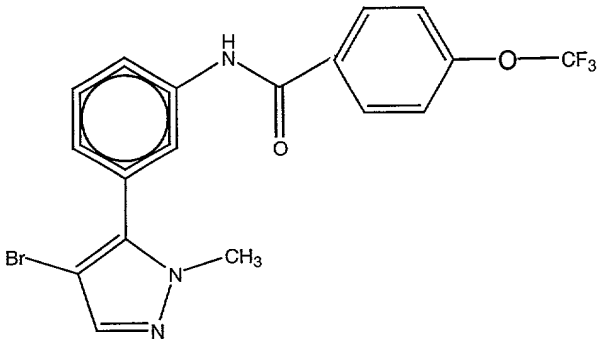

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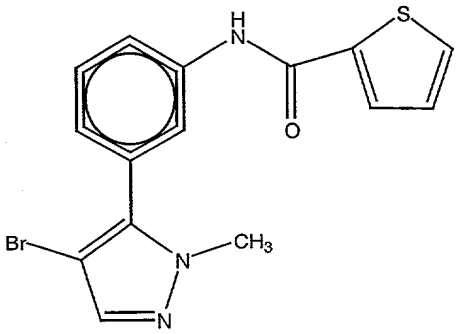

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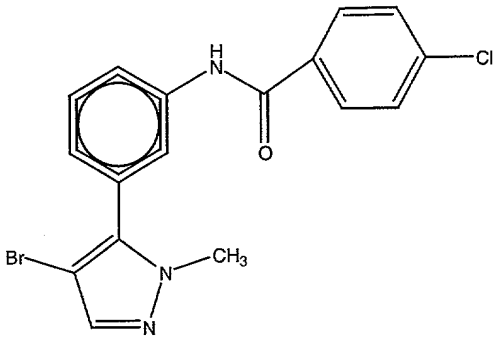
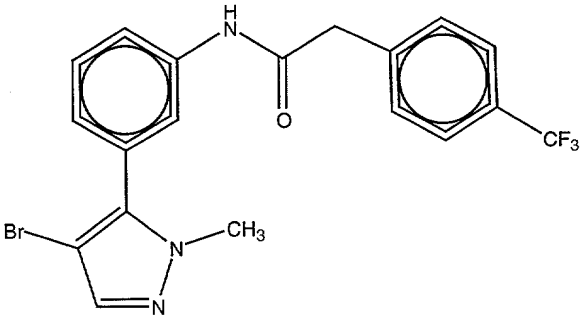
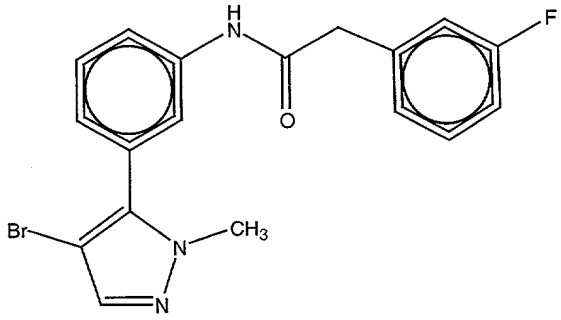

H
N
O
Cl
Br
N
CH3
N

,


H
N
O
CF3
Br
N
CH3
N

,


H
N
O
F
Br
N
CH3
N

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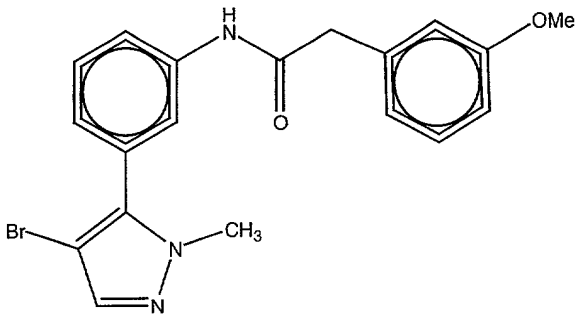
H
N
OMe
O
Br
N
CH3
N

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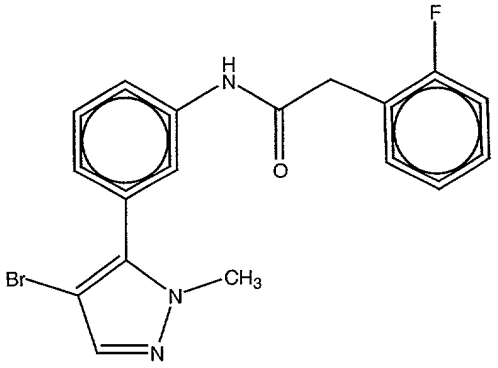
F
H
N
O
Br
N
CH3
N

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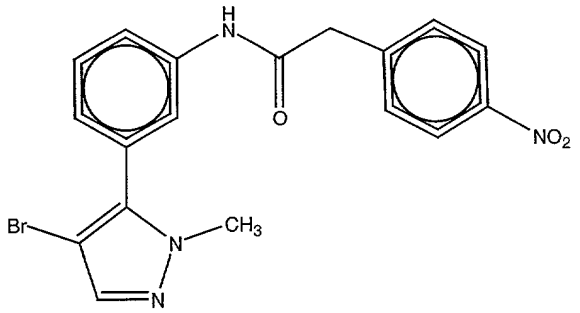
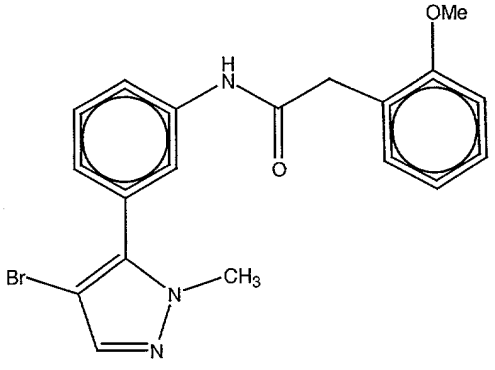

H
N
O
NO2
Br
N
CH3
N

, or


OMe
H
N
O
Br
N
CH3
N

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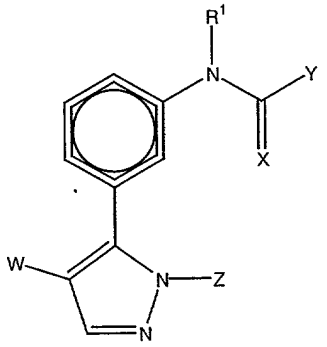
20. **(New)** A compound of formula (C):



(C)

Wherein:

W is Me, or Et, or halogen;

X is either Oxygen or Sulfur;

Y is NR^2R^3, or $(CH2)_m R^4$, or $O(CH_2)_n R^4$;

Z is lower alkyl (C_{1-6});

m=0-4;

n=0-4;

R^1 is H or lower alkyl (C_{1-4});

R^2 is H or lower alkyl(C_{1-4});

R^3 is a C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or $(CH_2)_k$ aryl group (k=1-4), and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, OCF_3, SMe, $COOR^7$, $SO_2NR^5R^6$, SO_3R^7, CO-lower alkyl, SCF_3 CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl,

aryl, and aryloxy wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, or aryloxy groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, $NHCOCH_3$, OCF3, SMe, $COOR^7$, SO_3R^7, $SO_2NR^5R^6$, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl;

R^4 is a C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, OCF_3, SMe, $COOR^7$, $SO_2NR^5R^6$, SO_3R^7, CO-lower alkyl, SCF_3 CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, and aryloxy wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, aryl, or aryloxy groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^5R^6$, NR^5R^6, $NHCOCH_3$, OCF3, SMe, $COOR^7$, SO_3R^7, $SO_2NR^5R^6$, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl;

R^5 and R^6 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH_2 aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^7R^8$, NR^7R^8, $NHCOCH_3$, OCF_3, SMe, $COOR^9$, SO_3R^7, $SO_2NR^7R^8$, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl wherein each of the C_{3-6} cycloalkyl, C_{1-6} alkyl, or aryl groups may be further optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, NO_2, OH, $CONR^8R^9$, NR^8R^9, $NHCOCH_3$, OCF_3, SMe, $COOR^7$, $SO_2NR^8R^9$, SO_3R^7, CO-lower alkyl, SCF_3, CN, C_{2-6} alkenyl, H, halogens, C_{1-4} alkoxy, C_{3-6} cycloalkyl, C_{1-6} alkyl, and aryl,

or R^5 and R^6 may form part of a 5, 6 or 7 membered cyclic structure which may be either saturated or unsaturated and that may contain up to four heteroatoms selected from O, N or S and said cyclic structure may be optionally substituted by up to four substituents in any position independently selected from CF_3, CCl_3, Me, NO_2, OH, OMe, OEt, OCF_3, SMe, $COOR^7$,

$SO_2NR^8R^9$, SO_3R^7, $NHCOCH_3$, COEt, COMe, or halogen;

R^7 may be independently selected from H or C_{1-6} alkyl;

R^8 and R^9 are independently a H, or C_{1-6} alkyl, or C_{2-6} alkenyl, or cycloalkyl, or aryl, or CH_2 aryl group and each said group may be optionally substituted by up to four substituents in any position independently selected from halogen, CF_3, OCF3, OEt, CCl_3, Me, NO_2, OH, OMe, SMe, COMe, CN, $COOR^7$, SO_3R^7, COEt, $NHCOCH_3$, or aryl;

an aryl moiety can be a 5 or 6 membered aromatic heterocyclic ring (containing up to 4 hetero atoms independently selected from N, O, or S) or a 6 membered aromatic non-heterocyclic ring or a polycycle;

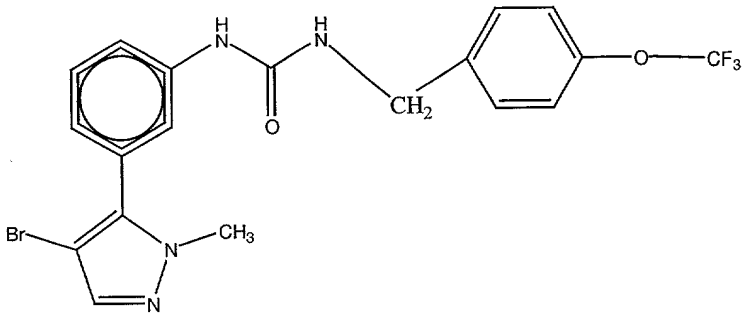
C_{1-6} alkyl moieties can be straight chain or branched;

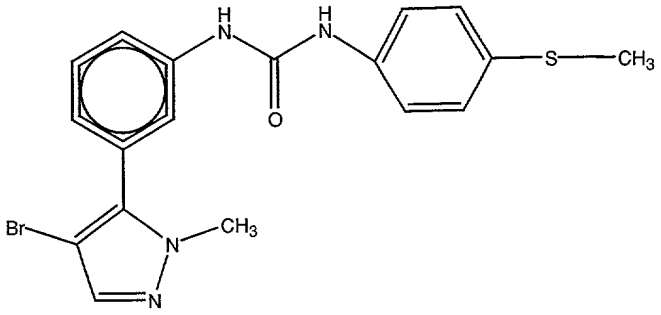
optionally substituted C_{1-6} alkyl moieties can be straight chain or branched;

C_{2-6} alkenyl moieties can be straight chain or branched; and

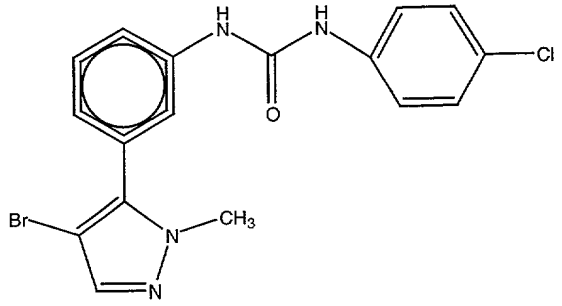
optionally substituted C_{2-6} alkenyl moieties can be straight chain or branched.

21. **(New)** A compound having a structure selected from the group consisting of:

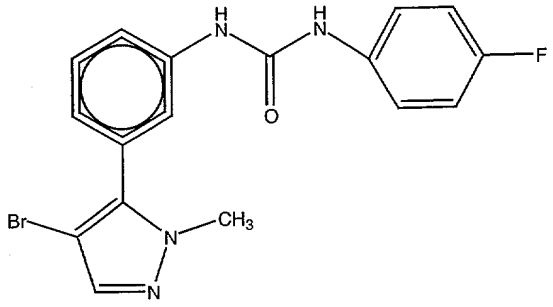



H
N
H
N
S
CH3
O
Br
N
CH3
N

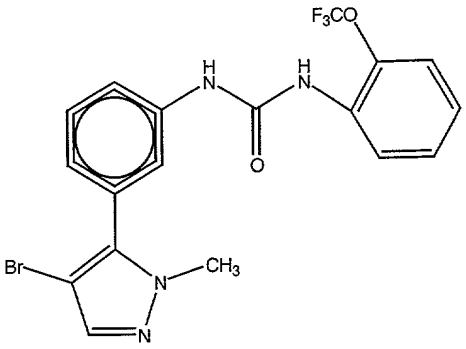
,


H
N
H
N
Cl
O
Br
N
CH3
N

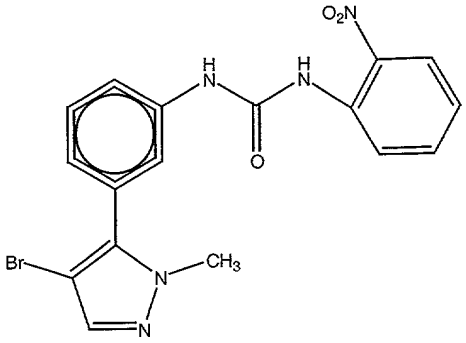
,


H
N
H
N
F
O
Br
N
CH3
N

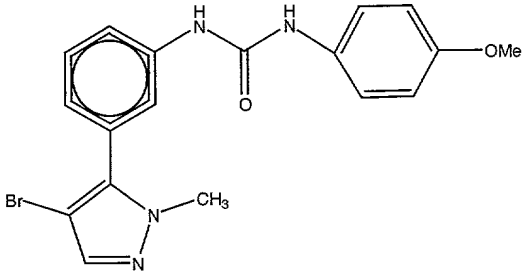
,


F3CO
H
N
H
N
O
Br
N
CH3
N

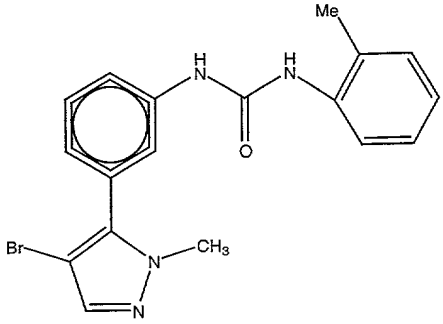
,


O2N
H
N
H
N
O
Br
N
CH3
N

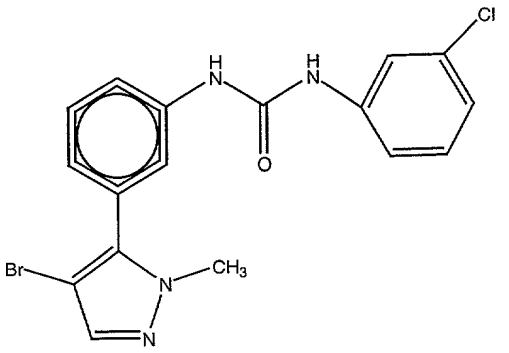
,


H
N
H
N
OMe
O
Br
N
CH3
N

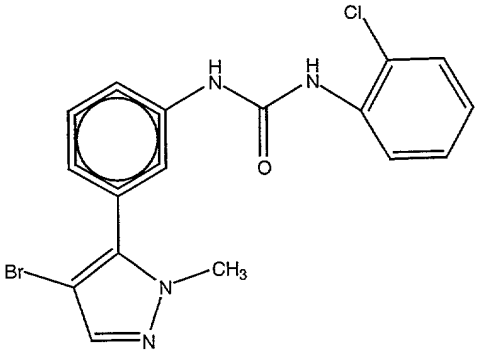
,


Me
H
N
H
N
O
Br
N
CH3
N

,


Cl
H
N
H
N
O
Br
N
CH3
N

,


Cl
H
N
H
N
O
Br
N
CH3
N

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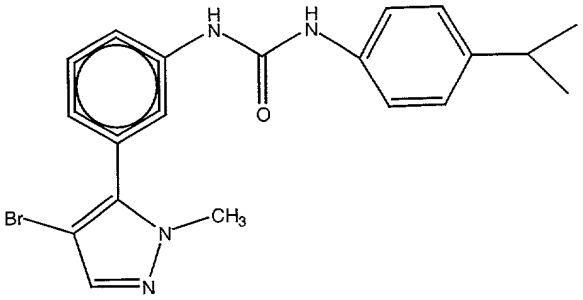
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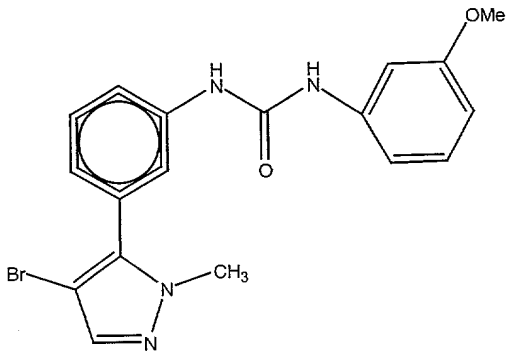
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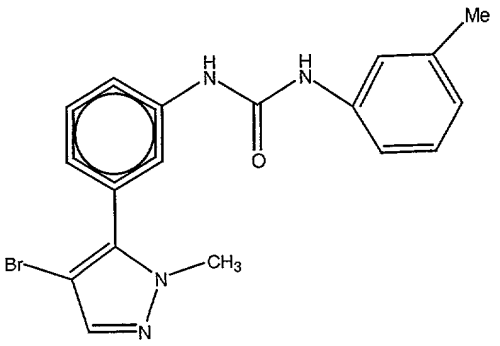
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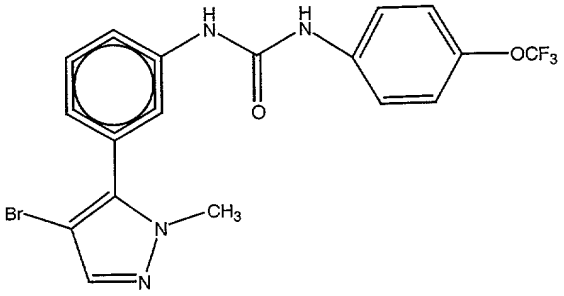
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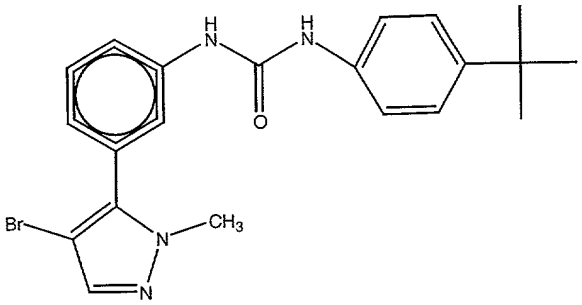
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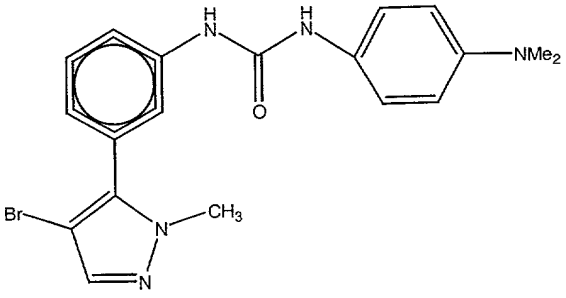
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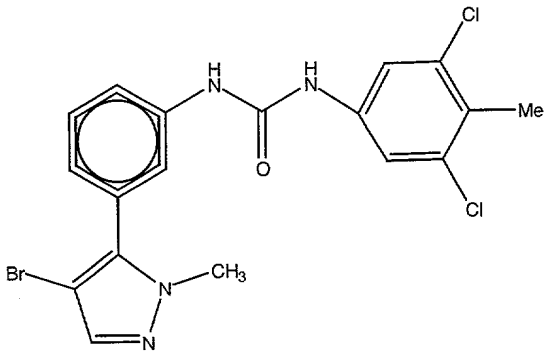
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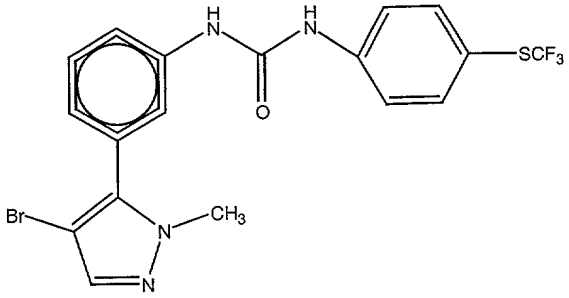
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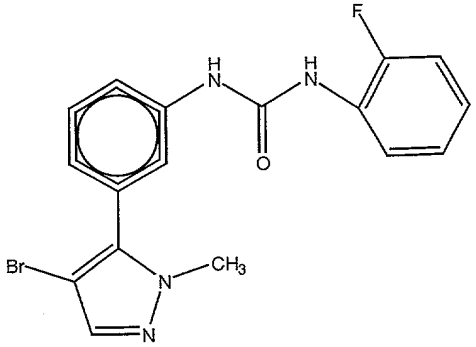
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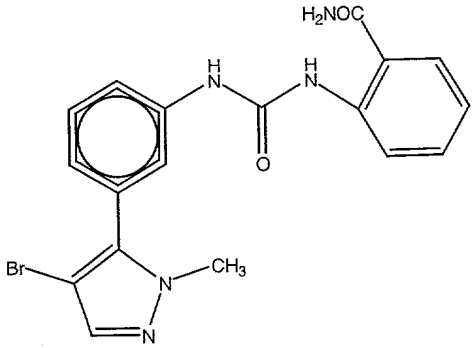
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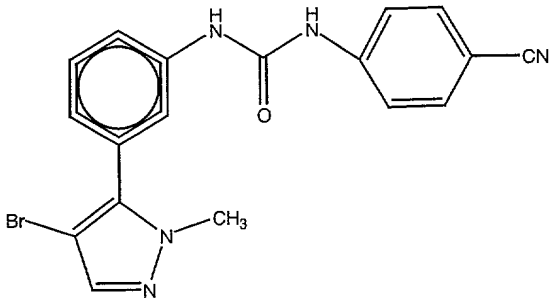

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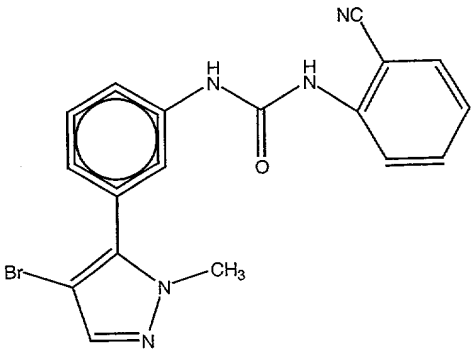

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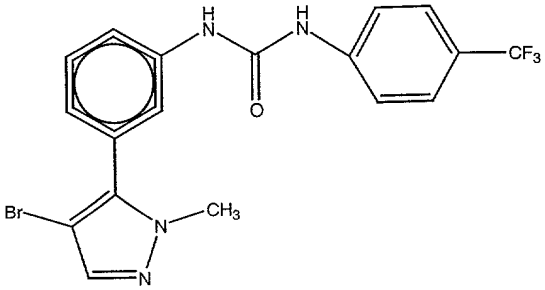

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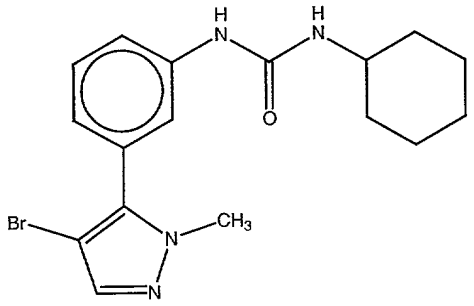

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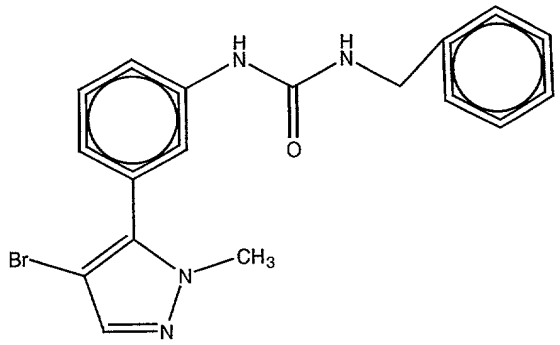

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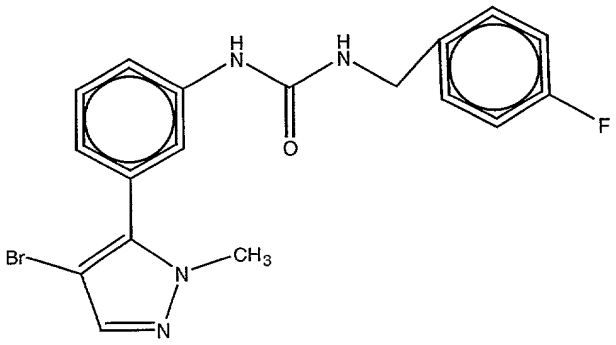

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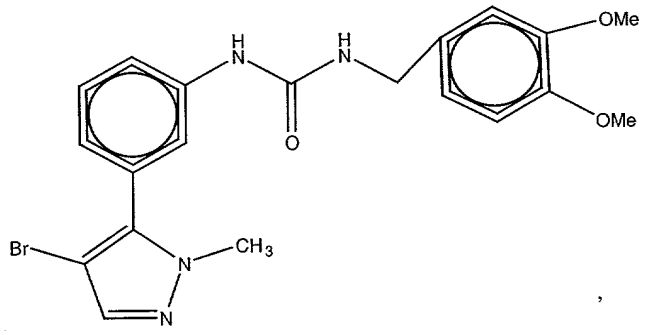

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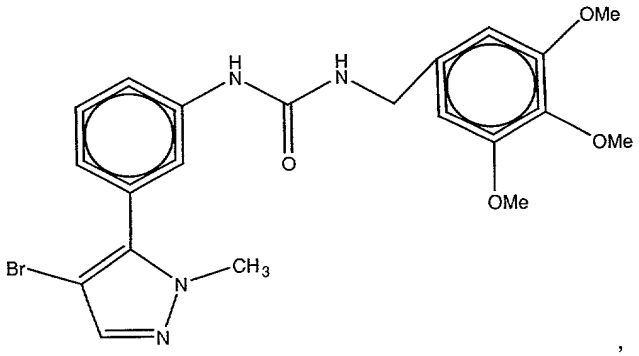

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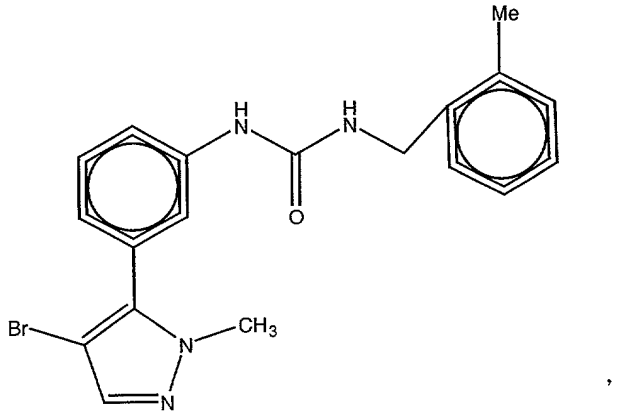
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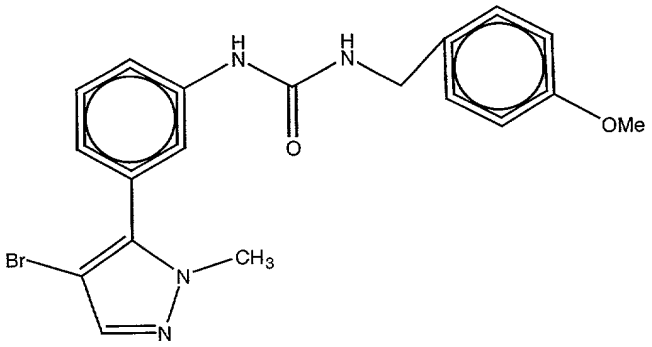
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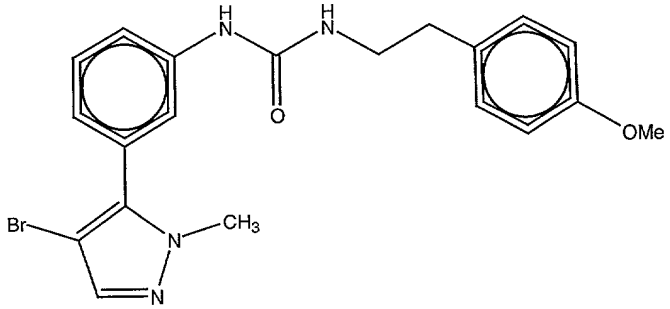
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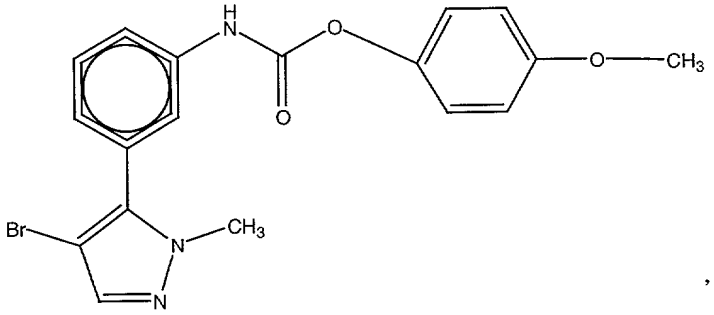
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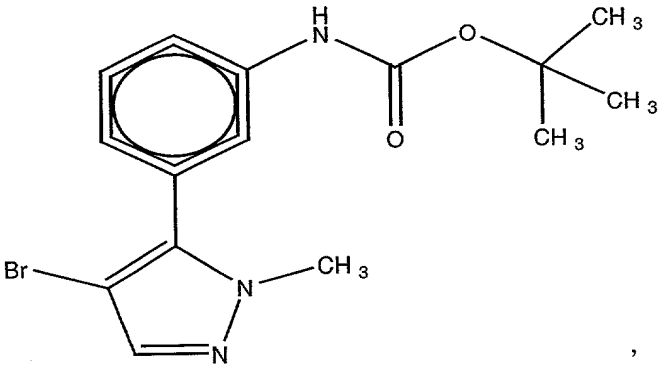

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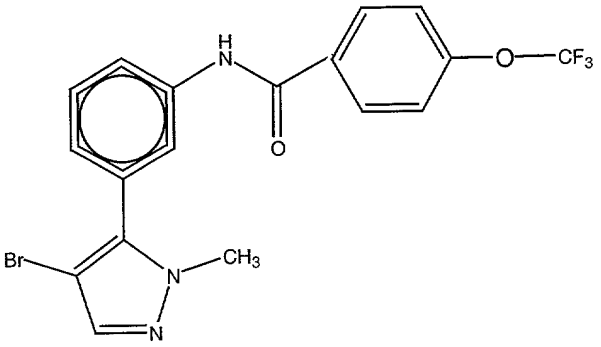

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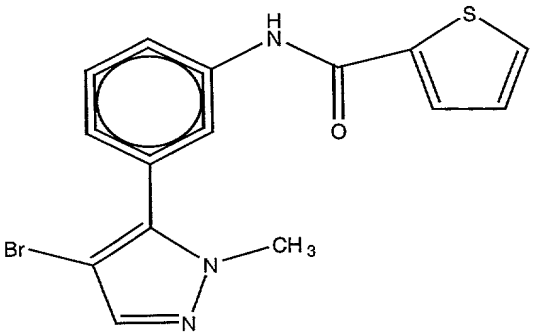

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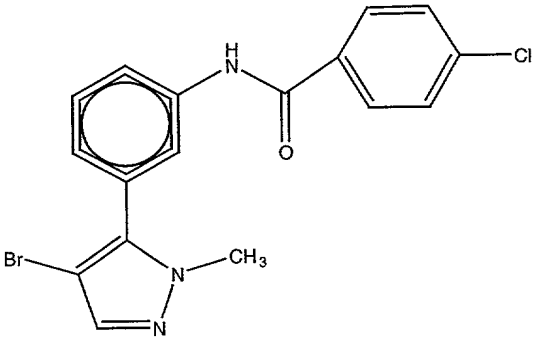
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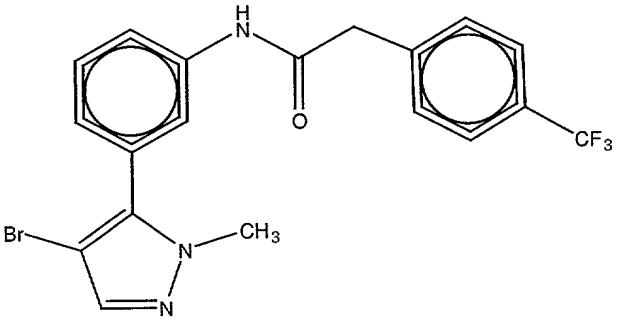
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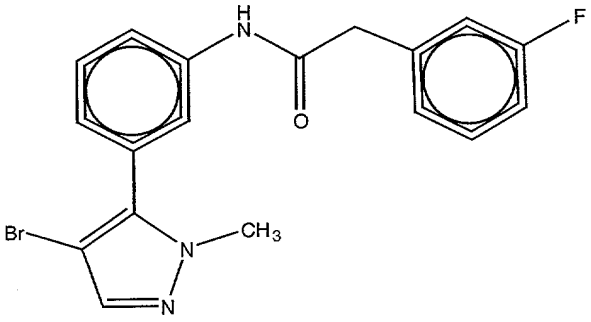
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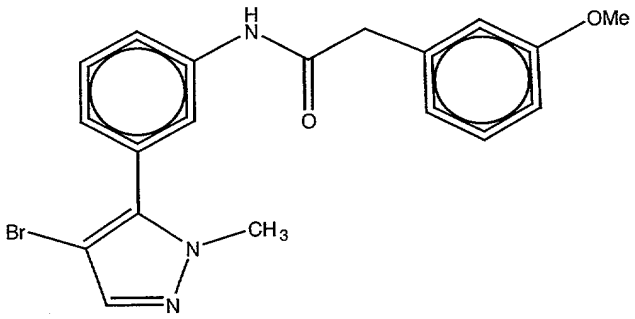
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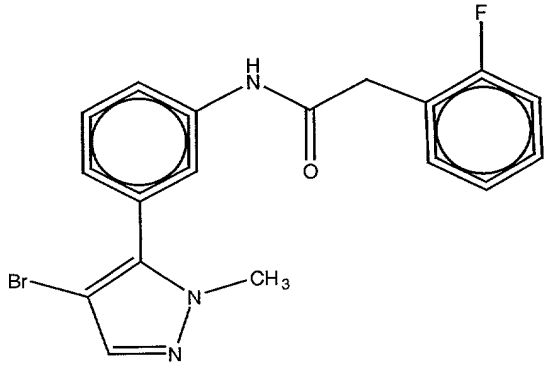
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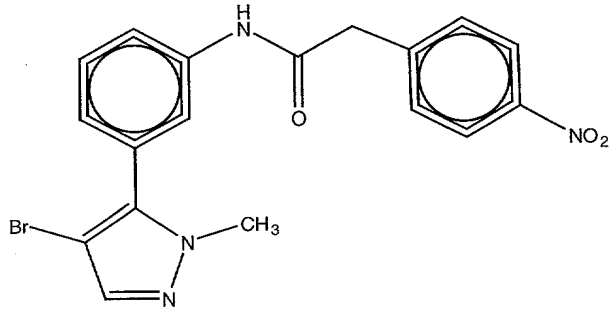
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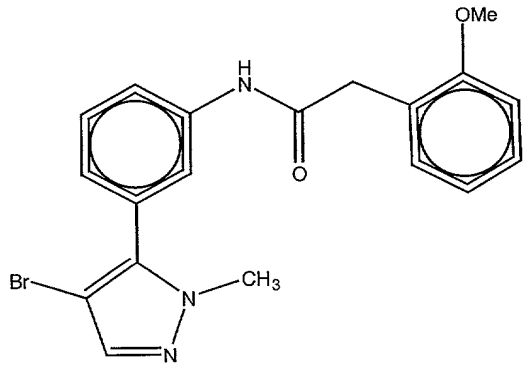
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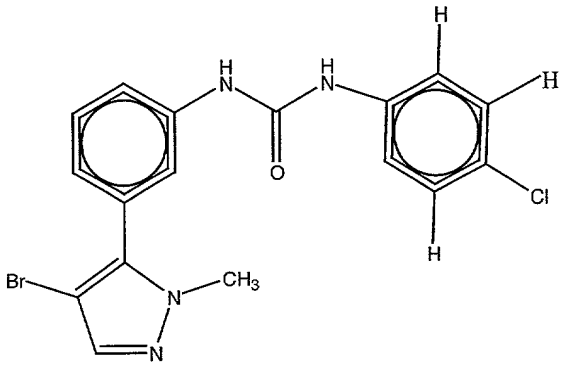
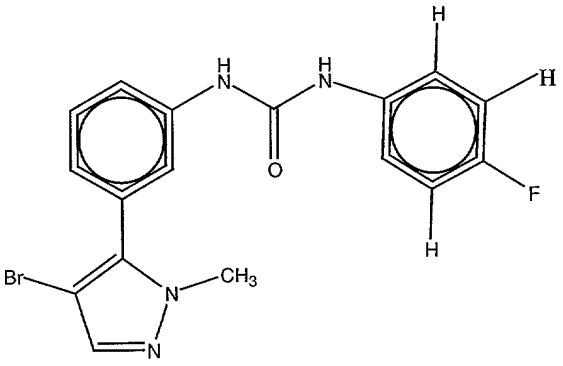
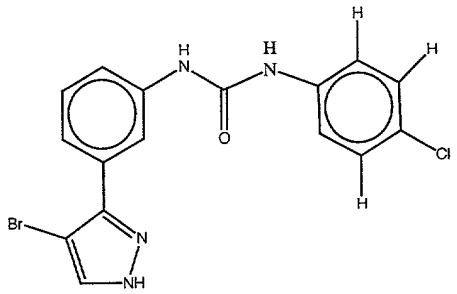
22. **(New)** A compound structurally represented as follows:



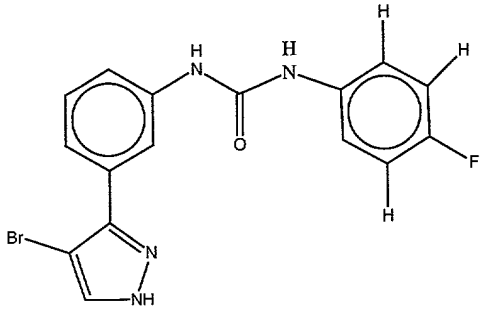
23. **(New)** A compound structurally represented as follows:



24. **(New)** A compound structurally represented as follows:



25. **(New)** A compound structurally represented as follows:



26 **(New)** A composition comprising a compound of any one of claims 21-25.